REVIEW DERLEME

Current View of Hemorrhagic Fever with Renal Syndrome in Adults and Children: an Overview

Yetişkinlerde ve Çocuklarda Renal Sendromlu Hemorajik Ateşin Güncel Görünümü: Genel Bir Bakış

Ilnur I Yagudin (0000-0002-6032-8839), Svetlana N Naidenkina (0000-0003-4359-5844), Margarita K Ermakova (0000-0001-8780-2994), Darya O Yagudina (0000-0003-3120-2994)

Izhevsk State Medical Academy Department of Pediatrics and Propedeutics of Childhood Diseases, Izhevsk, Russia

Cite this article as: Yagudin II, Naidenkina SN, Ermakova MK, Yagudina DO. Current view of hemorrhagic fever with renal syndrome in adults and children: an overview. J Curr Pediatr. 2025;23:50-6

Abstract

The review is devoted to hemorrhagic fever with renal syndrome (HFRS), analyzing studies on pathogenesis, etiology, diagnosis and treatment. The results of clinical features of the disease manifestation in children, as well as preventive measures aimed at reducing the disease in children are analyzed for the first time. The data on the available treatment of young patients were analyzed.

Öz

Bu derleme, patogenez, etiyoloji, tanı ve tedavi ile ilgili çalışmaları analiz ederek renal sendromlu hemorajik ateşe (HFRS) ayrılmıştır. Çocuklarda hastalık tezahürünün klinik özelliklerinin sonuçları ve çocuklarda hastalığı azaltmaya yönelik önleyici tedbirler ilk kez analiz edilmiştir. Genç hastaların mevcut tedavisine ilişkin veriler analiz edilmiştir.

Keywords
HFRS, children, diagnosis, treatment.

Anahtar kelimeler
HFRS, çocuklar, tanı, tedavi

Received/Geliş Tarihi : 04.05.2024
Accepted/Kabul Tarihi : 26.01.2025
Published Date/ Yayınlanma Tarihi : 09.04.2025

DOI:10.4274/jcp.2025.62134

Address for Correspondence/Yazışma Adresi: Bay Ilnur I Yagudin, Izhevsk State Medical Academy Department of Pediatrics and Propedeutics of Childhood Diseases, Izhevsk, Russia

E-mail: yagudin-ilnur@bk.ru

Introduction

Hemorrhagic fever with renal syndrome (HFRS) is a viral disease caused by the hantavirus genus, family Bunyaviridae. The disease is a zoonosis, and the field mouse (Apodemus agraricus) is considered to be a vector of viruses. It should be noted that there are studies proving that other mammals can also carry this infection (1). The virus is transmitted by biological secretions of the field mouse, namely saliva, feces and urine (2). The disease is not currently widespread on a territorial scale, but there is an annual increase in the number of cases, and this is due to the peculiarities of the infectious reservoir of HFRS (3).

Epidemiology

The increase and lack of decrease in the incidence of HFRS depends on the fact that rodents have the opportunity to be in close contact with humans. This is related to the diet of field mice, whose diet includes

the consumption of cereal plants, which causes them to enter human dwellings in search of food. After consumption, they leave their biological waste in the cereal tanks, thus human contact with rodent excretions occurs, which leads to human infection with Hantavirus (4). Mass field work has also become one of the variants of infection (5). In today's world, field and farm work is done by industrial organizations that use autonomous-specialized equipment, comb pared to years past, where manual labor of workers was previously used. The use of modern equipment, personal protective equipment, has reduced human contact with field mice and their biological secretions, which in turn has reduced the incidence of this pathology. Also, with the development of modern organization of health care and improvement of the quality of medical care, it became possible to better and competent diagnosis of HFRS in organizations where there is a risk of infection with this pathology, and also allowed better diagnosis of the pathology in conditions of civil medicine (6). One of the factors that has reduced the incidence of HFRS is the concentration of the population in cities, which allows people to move away from private homes, as rodents use human homes not only as a place to find food, but also as a warm and comfortable place to live. It should also be noted that at the moment there is supporting evidence that hantaviruses can be carried not only by rodents, but also by other mammals, including bats (7). There is statistical data confirming an increase in the incidence of HFRS in patients during the spring and fall seasons. It should be noted that the incidence of this pathology increases from year to year.

Virus Morphology

HFRS is a viral disease which is caused by a whole family of viruses, which includes such viruses as: Hantaan virus (HTNV), Amur virus (AMV), Seoul virus (SEOV), Dobrava virus (DOBV), Puumal virus (PUUV). An important feature is that these viruses are capable of causing disease of varying severity. There are studies demonstrating that with different species diversity of Bunyaviridae viruses, the disease has different degrees of severity (8). It should also be noted that the studies are not numerous and require further study and consideration. The viruses themselves are enveloped RNA-containing spherical viruses with a diameter of 80 to 120 nm and form a separate genus in the family Bunyaviridae (9). The genome consists of three single-stranded RNAs with a negative sense that share a common 3'-end sequence of genome segments. S (small), M (medium) and L (large) segments, encode nucleoprotein (N), envelope glycoproteins (Gn and Gc), and protein L or viral RNA-dependent RNA polymerase, respectively (10-12). The morphology of this virus allows it to tolerate high temperatures, thereby allowing the infection to persist in an aggressive environment. Despite this, the virus is easily killed when heated to 60 C ° for 30 minutes, exposed to UV irradiation and using organic solvents (13). This fact makes it possible to control the virus using specialized equipment, as well as to use personal protective equipment for humans, which in turn will reduce the risk of human exposure to infecting agents. In most cases, chemical agents are still used to kill rodents (14). These methods can help to limit the spread of the virus, but cannot eliminate it completely. It is very difficult to completely get rid of, or reduce the epidemiological zones, because anyway man will always be closely connected with nature, and regardless of the technological progress mankind will not be able to give up agricultural production, and completely get rid of interaction with animals, so this disease will exist and change, thus people will be interested in treatment for a long time. Based on existing studies, analyzing dangerous epidemiological areas, there are results in which the incidence remains high from year to year. It is important that in these areas' methods are used to control the virus, but the epidemiological zones are not reduced and the incidence is not reduced.

Pathogenesis is Associated with Changes in Hemodynamics

The pathogenesis of HFRS disease is not fully discovered, but there are already studies that have come close to deciphering this pathology. Hantavirus enters the human body through biological secretions of rodents, then the virus enters human cells through the respiratory and digestive systems, less often through the mucous membrane of the eyes (15,16). The damaging factor, namely inflammation, targets vascular endothelial cells, which in turn impairs their permeability, resulting in leakage from the bloodstream (17). There are studies that prove that the severity and the course of the disease depends on different associations of hantavirus RNA load (18). An

analysis of renal biopsies obtained from infected and uninfected patients was performed, concluding that intercellular contacts of the ZO-1 compound located in glomerular and tubointerstitial cells were impaired in infected patients. It is also important that the values of peptide reduction in cells correlate with the severity of clinical symptoms. Undoubtedly, the recovery of patients from hantavirus-induced HFRS, as well as other viral diseases, depends almost entirely on the immunological activity of the organism. Therefore, the pathogenesis is completely associated, with the action of the complement system, T-cell response, B-cells, and cytokine production, where everything and leads to the phenomenon of cytokine storm (19). This theory has already been supported by multiple studies describing those bioactive substances produced by macrophages, monocytes and lymphocytes in response to an inflammatory agent are involved in the regulation and activation of inflammation (20). There are studies demonstrating that during the febrile, hypotensive and oliguric period, serum concentrations of TNF-α, IL-6, IFN-γ, IL-8, IP-10 and RANTS are increased in the blood, and their levels are directly related to the severity of clinical symptoms. Thus, it was concluded that cytokines, namely TNF-α, IL-1 and IL-6, are mediators that lead to febrile syndrome, septic shock, as well as due to them increased production of acute phase proteins. There have been results highlighting that the cytokine IFN-β has the ability to act on endothelial cells, increasing the permeability of the vessel wall. IFN-β type I (IFN-β α/β) this cytokine is produced during viral infection, in proof there are studies that in vivo and in vitro showed that IFN-β is increased in serum (21). Another representative of cytokines is IFN-γ, the concentration of which also increases with the manifestation of the disease, so the dependence of the concentration, the manifestation of clinical symptoms, and the severity of the disease was investigated, resulting in a direct correlation of indicators (22). In the overall totality of the results obtained, a protective function of the immune system, represented by the cytokine storm, which is aimed at the elimination of the virus from the body, but at the same time is itself a manifestation of immunopathology, which also damages the body itself, is indeed observed. This defensive reaction leads to general clinical syndromes in the body: general toxic, hemodynamic disorders, acute renal failure, disseminated intravascular coagulation, abdominal (dyspeptic) syndrome and respiratory syndrome (23). Thus, when the immune response gets out of control, it leads to irreversible consequences in the body.

Clinic of the Disease

Infection of humans with the virus that causes HFRS occurs through inhalation of virus-containing aerosols released from rodent excretions, such as urine, feces, and saliva. In this way, the virus is transmitted by airborne droplets and spreads in the body. Infection and the disease process are divided into clinical periods: incubation, febrile, hypotensive shock, oliguric, polyuric, and recuperative periods. The incubation period may take 1-5 weeks. The next period is febrile, which lasts 3 to 5 days, manifesting itself by clinical symptoms such as fever, chills, thirst, cough, muscle and joint pain, which are not characteristic of a particular disease, so in practice these symptoms are usually written off as acute respiratory diseases (ARI). The key moment comes when the manifestation of hemorrhagic syndrome is determined, which in turn is represented by a petechial rash. All the listed manifestations vary and there is no clear gradation. Further, the course of the disease progresses to hypotensive shock, it lasts from several hours to several days. This period is very important in treatment, as it requires special attention and monitoring the dynamics of blood pressure, as it can rapidly fall to low values, which in turn aggravates the patient, as low blood pressure in combination with inflammatory renal damage closes in a pathological circle, which leads to deep kidney damage. The oliguric period (3 to 7 days), is, according to numerous studies, the most fatal, as patients die predominantly during this period (24). It is essential that all pathological manifestations reach their maximum, namely, general toxic manifestations, hemodynamic disorders, renal failure, etc in this period. Then there comes a period that leads to the resolution of the disease is polyuric (1-2 weeks). Here the pain disappears, sleep and appetite normalize, and diuresis resumes. All this is aimed to improve the patient's condition. And the final distinguished period is the period of recuperation (3-6 months), as pathological processes subside, laboratory parameters such as creatinine and urea are normalized. It is important to understand that acute condition caused by HFRS can lead to the development of non-cardiogenic pulmonary

edema, pathological development is directed towards ARDS, which closes with the death of the patient. The time and transition from one stage to another, depends not only on different hantavirus serotypes, but also depends on compensatory and individual body characteristics. Currently, there are no existing methods that can predict the exact stage and guarantee the transition from one to another, so there is a need for a more accurate differential diagnosis of the disease, and an increase in the speed of obtaining test results. A study was conducted to analysis the medical histories of children with HFRS and compare symptoms in children with adults to identify the characteristics of the disease. The result was similarity of symptoms with adult patients (25).

Markers in the Diagnosis of HFRS

In scientific studies related to HFRS disease, a lot of data was obtained, namely, a new feature of more in-depth pathogenesis was revealed, as a precursor of natriuretic hormone called NTproBNP peptide was identified (26). It was possible to achieve the detection of NTproBNP peptide in the blood, thus it became possible to focus on the concentration of this peptide and analyze the degree of damage to the body, as well as to use as a diagnostic marker in the disease of HFRS (27). In essence, this peptide has become a marker that can now be used in the diagnosis of the disease and used to analyze the disease. This peptide is released in response to renal and cardiac damage. This peptide is known to be elevated during all periods of HFRS disease, but its maximum serum concentration is reached during the oliguric period. This is due to the fact that NTproBNP peptide is produced by heart cells in order to reduce the hemodynamic load on the heart (28,29). This may be due to the fact that during the disease of HFRS in conjunction with pathological syndromes, there is hemorrhage in the right atrial auricle, which provokes receptors for the production of the peptide. It should be noted that the manifestation of renal pathology also leads to retention of NTproBNP peptide, which increases its concentration in the blood as its excretion from the body is impaired. (30). Thus, the manifestation of cardiorenal syndrome type 3 leads to an increase in serum peptide concentration. Currently, studies have been carried out investigating the effect of clotting system and folate cycle gene polymorphism on echocardiographic parameters in HFRS (31). The F7:10976 G/A gene polymorphism is known to decrease gene expression, resulting in lower levels of factor VII, which is used as a marker of thrombosis formation and myocardial infarction. Thus, it was revealed that allele a of F7:10976 G/A gene was detected more often in patients with developed signs of thromboendocarditis, and genotype G/G of FGB: -455G/A gene was often detected in myocardial longitudinal peak strain disorder. Thus, it is possible to distinguish and diagnose each period, as well as to analyze and speak about the patient's prognosis. Due to competent analysis and identification of patterns, a new marker of HFRS, which is a biological component of the body (peptide), has been identified, which allows to diagnose the disease without using external substances for diagnosis without infusion. Therefore, this fact may allow improving the quality and speed of diagnosis of HFRS. Despite already having disease markers that were detected at different periods of the disease, they can fall out of the cycle and also overlap with each other, which in turn certainly blurs the clinical picture. These features are important when choosing the right treatment tactics.

Diagnosis of HFRS with an Emphasis on Instrumental Methods of Investigation

The most important thing in the practice of any clinician is an early diagnosis, because it is early diagnosis that will solve the patient's problem with lower consequences, namely damage to organs and systems, and increase the likelihood of complete recovery. Therefore, it is very important to identify the patient as early as possible and begin specialized treatment of the patient. It is known that everything is not limited to one method, there are also used laboratory methods (biochemical, serological), electrocardiography (ECG), chest radiography in direct projection, renal ultrasound, and determination of oxygen saturation (SpO_2) using pulse oximeter (32-35). Further, it is necessary to expand on the above studies. The use of the biochemical blood test is more general, and indicates general inflammation despite the fact that the spectrum is much broader compared to the general blood test, clear detection of the virus is not detected. Therefore, in such a case, a serological method of investigation is further used, which in turn allows definitive confirmation and

identification of the virus that causes HFRS (36). Discoveries in the field of HFRS diagnosis do not stand still, so there is a development of this direction and research in this area. A patent has been received for a method that makes it possible to increase the accuracy, speed and quality of HFRS diagnosis at early stages (RU Patent 2735810). This invention allows to carry out a diagnosis of HFRS, using the results of research, which are based on syndromes, such as fever, hemorrhagic syndrome, urinary syndrome and using ultrasound elastometry method allows to make an accurate diagnosis quickly, namely by determining the stiffness of the renal parenchyma when the stiffness value is below 16 kPa, and if the patient has the syndromes listed above, then the patient can be diagnosed with hemorrhagic fever with renal syndrome. And if the stiffness is above 16 kPa, then the diagnosis cannot be HFRS. The presented method development bears unique properties, namely that the method is very cheap and easy to use, as it does not use expensive equipment. This method makes it possible to increase the speed of diagnosis, as well as to use it in hospitals that are less financed and thus have less equipment. Therefore, this method is already recognized and used in practice.

Treatment

HFRS carries many features that need to be considered in the treatment of this disease. The following treatments and studies were conducted on adult patients. There are many drugs that can be used in treatment, namely, including IFN-α, steroids, and cyclophosphamide, they have been shown to be effective in improving the condition of patients (37,38). It is also important to understand that special attention needs to be given to the patient by equalizing the water-salt balance, as due to the implications of the clinic, this is the primary goal in stabilizing the patient during the disease (39). One of the antiviral drugs ribavirin (1-beta-D-ribofuranosi-11,2,4-triazole-3-carboxamide) was used in the treatment of patients, and it was found that for the best effectiveness of the drug it is necessary to start treatment as early as possible, this allows achieving a rapid recovery, but also an important feature that with its use the mortality of patients was higher (40). New monoclonal antibodies (MAbs), which have shown good results in trials, are a hope to improve the effectiveness of HFRS therapy (41). An important problem is that there is no specific treatment for children, so the treatment of patients is only symptomatic.

Prevention

HFRS is a very common pathology, thus it remains a current problem in epidemiology. As we already know, the way of infection is practically figured out. At the moment we know how to fight it, namely to use individual means of protection, to protect one's home from rodents to use poisonous substances (42-44). All this is used by the population and it is also important to carry out sanitary-educational measures for the population, which allowed to increase the safety of the population in epidemiological foci. These measures already exist and in most cases are used, but the infection of the population still occurs, so they are not the key to solve the problem. Therefore, all hope of preventing HFRS should be directed to vaccination of the population, which would allow to receive protection properly. In connection with this, a Hantavax vaccine was developed in China (Korea Green Cross, Seoul, Korea), which was based on dead Hantavirus DNA, this was derived from the brain of infected rodents, but its effectiveness tended to zero over time, and eventually became completely useless (45-47).

Conclusion

As a result, HFRS remains and will continue to be an urgent problem for which a lot of effort will have to be put into finding a solution, also the pathogenesis of the disease will have to be fully studied, and new methods of individual protection, chemical substances, with higher effectiveness and greater humanity to the reservoirs of the virus will have to be invented. This would help reduce transmission in humans and would have a major impact on reducing the incidence of the disease. The development of new drugs would produce more effective results, thereby improving the therapy for HFRS disease. Creation of a working vaccine would lead to the development of general immunity in the population, could lead to a complete victory over the problem. Therefore, it is necessary to work together with the entire scientific community to achieve these results in the future.

Ethics

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Avšič-Županc T, Saksida A, Korva M. Hantavirus infections. Clin Microbiol Infect. 2019;21:e6-16.
2. Riquelme R. Hantavirus. Semin Respir Crit Care Med. 2021;42:822-7.
3. Jiang H, Zheng X, Wang L, Du H, Wang P, Bai X. Hantavirus infection: a global zoonotic challenge. Virol Sin. 2017;32:32-43.
4. Tian H, Stenseth NC. The ecological dynamics of hantavirus diseases: from environmental variability to disease prevention largely based on data from China. PLoS Negl Trop Dis. 2019;13:e0006901.
5. Amaral CD, Costa GB, de Souza WM, Alves PA, Borges IA, Tolardo AL, et al. Silent orthohantavirus circulation among humans and small mammals from central minas gerais, Brazil. Ecohealth. 2018;15:577-89.
6. Zhang R, Mao Z, Yang J, Liu S, Liu Y, Qin S, et al. The changing epidemiology of hemorrhagic fever with renal syndrome in Southeastern China during 1963-2020: a retrospective analysis of surveillance data. PLoS Negl Trop Dis. 2021;15:e0009673.
7. Sabino-Santos G Jr, Maia FGM, Martins RB, Gagliardi TB, Souza WM, Muylaert RL, et al. Natural infection of neotropical bats with hantavirus in Brazil. Sci Rep. 2018;8:9018.
8. Tariq M, Kim DM. Hemorrhagic fever with renal syndrome: literature review, epidemiology, clinical picture and pathogenesis. Infect Chemother. 2022;54:1-19.
9. Gu SH, Kumar M, Sikorska B, Hejduk J, Markowski J, Markowski M, et al. Isolation and partial characterization of a highly divergent lineage of hantavirus from the European mole (Talpa europaea). Sci Rep. 2016;6:21119.
10. Wang N, Yin JX, Zhang Y, Wu L, Li WH, Luo YY, et al. Genetic evolution analysis and host characteristics of hantavirus in yunnan province, china. Int J Environ Res Public Health. 2022;19:13433.
11. Singh S, Numan A, Sharma D, Shukla R, Alexander A, Jain GK, et al. Epidemiology, virology and clinical aspects of hantavirus infections: an overview. Int J Environ Health Res. 2022;32:1815-26.
12. Serris A, Stass R, Bignon EA, Muena NA, Manuguerra JC, Jangra RK, et al. The hantavirus surface glycoprotein lattice and its fusion control mechanism. Cell. 2020;183:442-56.
13. Kallio ER, Klingström J, Gustafsson E, Manni T, Vaheri A, Henttonen H, et al. Prolonged survival of puumala hantavirus outside the host: evidence for indirect transmission via the environment. J Gen Virol. 2006;87:2127-34.
14. Dheerasekara K, Sumathipala S, Muthugala R. Hantavirus infections-treatment and prevention. Curr Treat Options Infect Dis. 2020;12:410-21.
15. Torriani G, Mayor J, Zimmer G, Kunz S, Rothenberger S, Engler O. Macropinocytosis contributes to hantavirus entry into human airway epithelial cells. Virology. 2019;531:57-68.
16. Lim SC, Lee YM, Kim CM, Yun NR, Kim DM. Acute appendicitis associated with hantaan virus infection. Am J Trop Med Hyg. 2021;105:801-6.
17. Jiang H, Du H, Wang LM, Wang PZ, Bai XF. Hemorrhagic fever with renal syndrome: pathogenesis and clinical picture. Front Cell Infect Microbiol. 2016;6:1.
18. Lu S, Zhu N, Guo W, Wang X, Li K, Yan J, et al. RNA-Seq Revealed a Circular RNA-microRNA-mRNA regulatory network in hantaan virus infection. Front Cell Infect Microbiol. 2020;10:97.
19. Garanina E, Martynova E, Davidyuk Y, Kabwe E, Ivanov K, Titova A, et al. Cytokine storm combined with humoral immune response defect in fatal hemorrhagic fever with renal syndrome case, tatarstan, Russia. Viruses. 2019;11:601.
20. Vangeti S, Strandin T, Liu S, Tauriainen J, Räisänen-Sokolowski A, Cabrera L, et al. Monocyte subset redistribution from blood to kidneys in patients with Puumala virus caused hemorrhagic fever with renal syndrome. PLoS Pathog. 2021;17:e1009400.
21. Jiang H, Wang PZ, Zhang Y, Xu Z, Sun L, Wang LM, et al. Hantaan virus induces toll-like receptor 4 expression, leading to enhanced production of beta interferon, interleukin-6 and tumor necrosis factor-alpha. Virology. 2008;380:52-9.
22. Khaiboullina SF, Martynova EV, Khamidullina ZL, Lapteva EV, Nikolaeva IV, Anokhin VV, et al. Upregulation of IFN-γ and IL-12 is associated with a milder form of hantavirus hemorrhagic fever with renal syndrome. Eur J Clin Microbiol Infect Dis. 2014;33:2149-56.
23. Borodina ZI, Tsarenko OY, Monakhov KM, Bagautdinova LI. Hemorrhagic fever with renal syndrome: the challenge of our time. The Russian Archives of Internal Medicine. 2019;9:419-27.
24. Wang WJ, Zhao J, Yang JS, Liang MM, Ni MY, Yang JH. Clinical analysis of patients with acute pancreatitis complicated with hemorrhagic fever with renal syndrome and acute biliary pancreatitis. Medicine (Baltimore). 2020;99:e18916.
25. Echterdiek F, Kitterer D, Alscher MD, Schwenger V, Ruckenbrod B, Bald M, et al. Clinical course of hantavirus-induced nephropathia epidemica in children compared to adults in Germany-analysis of 317 patients. Pediatr Nephrol. 2019;34:1247-52.
26. Manakhov KM, Bagautdinova LI, Malinin OV, Dudarev MV, Sarksyan DS, Ivanov VG, et al. Dynamics of n-terminal fragment of the brain natriuretic peptide precursor serum concentration in patients with hemorrhagic fever with renal syndrome. Bashkortostan medical journal. 2021;16:5-11.
27. Rajaniemi SM, Hautala N, Sironen T, Vainio O, Vapalahti O, Vaheri A, et al. Plasma B-type natriuretic peptide (BNP) in acute puumala hantavirus infection. Ann Med. 2014;46:38-43.
28. Rasmuson J, Lindqvist P, Sörensen K, Hedström M, Blomberg A, Ahlm C. Cardiopulmonary involvement in puumala hantavirus infection. BMC Infect Dis. 2013;13:501.
29. Fan J, Ma J, Xia N, Sun L, Li B, Liu H. Clinical value of combined detection of CK-MB, MYO, cTnI and Plasma NT-proBNP in diagnosis of acute myocardial infarction. Clin Lab. 2017;63:427-33.

30. Santaguida PL, Don-Wauchope AC, Oremus M, McKelvie R, Ali U, Hill SA, et al. BNP and NT-proBNP as prognostic markers in persons with acute decompensated heart failure: a systematic review. Heart Fail Rev. 2014;19:453-70.
31. Manakhov KM, Sarksyan DS, Dudarev MV, Chernobrovkina M, Pribytkova PY, Filimonova SV. Gene polymorphism in blood coagulation system and folate cycle affecting heart condition in patients with hemorrhagic fever and renal syndrome. Russian Journal of Infection and Immunity. 2022;12:347-56.
32. Lebecque O, Falticeanu A, Mulquin N, Dupont M. Abdominal CT findings in Puumala hantavirus-infected patients. Abdom Radiol (NY). 2022;47:2552-9.
33. Teng AY, Che TL, Zhang AR, Zhang YY, Xu Q, Wang T, et al. Mapping the viruses belonging to the order Bunyavirales in China. Infect Dis Poverty. 2022;11:81.
34. Prince HE, Lieberman JM. Impact of the Yosemite hantavirus outbreak on hantavirus antibody testing at a national reference laboratory. Clin Vaccine Immunol. 2013;20:1213-6.
35. Galieva GA, Mirsaeva GK, Fazlyeva RM. Comparative study of myocardial damage in hantavirus and new coronavirus infection. Meditsinskiy Sovet. 2023;17:44-50.
36. Chau R, Bhatt N, Manhiça I, Cândido S, de Deus N, Guiliche O, et al. First serological evidence of hantavirus among febrile patients in Mozambique. Int J Infect Dis. 2017;61:51-5.
37. Brocato RL, Hooper JW. Progress on the Prevention and Treatment of Hantavirus Disease. Viruses. 2019;11:610.
38. Mittler E, Dieterle ME, Kleinfelter LM, Slough MM, Chandran K, Jangra RK. Hantavirus entry: perspectives and recent advances. Adv Virus Res. 2019;104:185-224.
39. Zhang D, Wang X, Lv J, Dong Y. Treatment of a patient with severe hemorrhagic fever accompanied by infection with methicillinresistant staphylococcus aureus, acinetobacter baumannii, aspergillus and mucor: a case report. Int J Clin Pharmacol Ther. 2015;53:1028-34.
40. Szabó R. Antiviral therapy and prevention against hantavirus infections. Acta Virol. 2017;61:3-12.
41. Duehr J, McMahon M, Williamson B, Amanat F, Durbin A, Hawman DW, et al. Neutralizing monoclonal antibodies against the gn and the gc of the andes virus glycoprotein spike complex protect from virus challenge in a preclinical hamster model. mBio. 2020;11:e00028-20.
42. Hansen A, Cameron S, Liu Q, Sun Y, Weinstein P, Williams C, et al. Transmission of haemorrhagic fever with renal syndrome in china and the role of climate factors: a review. Int J Infect Dis. 2015;33:212-8.
43. Rubio AV, Fredes F, Simonetti JA. Exotic pinus radiata plantations do not increase andes hantavirus prevalence in rodents. Ecohealth. 2019;16:659-70.
44. Tosa N, Ishida T, Yoshimatsu K, Hayashimoto N, Shiokawa K, Takakura A, et al. Simultaneous serodetection of major rat infectious pathogens by a multiplex immunochromatographic assay. Exp Anim. 2021;70:161-8.
45. Song JY, Jeong HW, Yun JW, Lee J, Woo HJ, Bae JY, et al. Immunogenicity and safety of a modified three-dose priming and booster schedule for the Hantaan virus vaccine (Hantavax): a multi-center phase III clinical trial in healthy adults. Vaccine. 2020;38:8016-23.
46. Khan A, Shin OS, Na J, Kim JK, Seong RK, Park MS, et al. A systems vaccinology approach reveals the mechanisms of immunogenic responses to hantavax vaccination in humans. Sci Rep. 2019;9:4760.
47. Bae JM. Introduction of vaccinomics to develop personalized vaccines in light of changes in the usage of hantaan virus vaccine (Hantavax®) in Korea. J Prev Med Public Health. 2019;52:277-80.