Analysis of the cases of Hantavirus in the United State to avoid the next outbreak

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Abstract. Hantaviruses have always existed in today's society, and people in many countries have been attacked by rodents, or unknowingly in contact with rodent fluids, leading to a silent increase in the number of hantavirus cases. Compared to the current COVID-19 epidemic, the hantavirus is not well known to the world, but in fact, not only in the United States but in China, HFPS cases account for more than half of the confirmed cases globally. Both HPS and HFPS can lead to severe clinical features such as hypotensive shock, renal failure, and other symptoms. At present, there is no specific medicine, and the vaccine technology is not mature. Vaccines are still in development and have not yet reached the ideal state. So, this essay is to summarize the past surveillance and control of the hantavirus in the United States to reduce the possibility of a resurgence of the virus. By explaining the cases of hantavirus in the United States and the work, race, gender, and many different aspects of the patients, the current treatment direction and methods of hantavirus are explained. On the whole, people should pay more attention to epidemic monitoring, strengthen customs management, strengthen people's awareness of the hantavirus, and strengthen education in high-risk areas, to be more able to control the outbreak of the epidemic.

Keywords: Hantavirus, United State, Next break, Hemorrhagic Fever with Renal Syndrome (HFRS), Hantavirus Pulmonary Syndrome (HPS).

1. Introduction

Since the epidemic has emerged, more and more people started to more focus on Hantavirus due to the internet. Because the internet become more and more developed, we can know more messages from other countries. In China, it had a very serious infection by Hantavirus from 2018 to 2020. Hantavirus appeared on the 20th and every year some people will be infected. In the beginning, it was just a group of American and United Nations soldiers in the Korean War and most soldiers had been infected with acute renal failure. Until now, there hasn't had any vaccine or effective way recognized by the WHO. As a virus that is Biosafety level4, it has severe symptoms in clinical, especially for kidney [1], and because the ecosystem continually changes so people have more and more chances of contact with the host which are mice. Different kinds of mice can transmit the virus and we had already known that 5 kinds of mice can carry the virus and about 21 kinds of viruses exist in our society. That is a very serious problem if there's a next outbreak of the virus, what should people need to do? From the two directions of successful and unsuccessful experience, what experience do people need to learn from? or what way needs to be changed to reduce the outbreak probability or death rate? The problem we are facing is not only that people lack awareness and knowledge of this virus, but also people always have a fluke mentality, so they think that some viruses are far away from us, but it is not, popular science is also a very important part. Hantavirus has appeared for many years, there were still outbreaks, and about 200,000 people were infected with Hantavirus every year and most of them are asymptomatic contacts, which also caused great security risks [2]. Therefore, people should start with known information to minimize the spread of the virus and to make sure whether is there any chance to minimize the outbreak appear.

2. Introducing Hantavirus

2.1. What is Hantavirus and the host

Hantaviruses are kinds of Bunyaviridae that have single-strand RNA (enveloped RNA virus) and are mainly transmitted by rodents and can cause two types of disease which are hemorrhagic fever with renal syndrome (HFRS) and Hantavirus pulmonary syndrome (HPS). It has many different genotypes, and the International Committee on Taxonomy of Viruses (ICTV) divides the virus into 4 subtypes that are Hantaan virus, Seoul virus, Puumala virus, and Dobrava virus [3]. Hantaviruses are broadly separated into two categories, New World viruses and Old-World viruses. HFRS, on the other hand, is mainly caused by Old World hantaviruses and is more specific to Asia, including some of the more prevalent strains. The ratio is as high as 15%. In history, there are two serious outbreaks in the world. From 1950 to 1953, The Korean war started and there are over 3000 United Nations troops sick because they had to drink unclean water. That was the first time find a hantavirus. Another one was in 1993, a very serious virus emerged in the United States where the cases were located in four corners of the southwestern United States, which was the first time that humans were discovered and infected countless people. That was mainly caused by the Sin Nombre hantavirus (SNV). SNV is the most significant reason cause the hantavirus. After that new type of virus appeared which led to a significant increase in the lethality rate of Hantavirus, HFPS reached 12% and HPS reached 60%. Andes virus (ANDV) is another causative agent of hantavirus. HFRS affects about 200,000 people in Asia every year, which also leads to a new world where the fatality rate of Hantavirus has increased dramatically, up to 50%, with about 300 cases per year in the Americas. For New World and Old-World viruses, which have different rodent hosts, there are three typical host types. HPFS is an old-world virus and HPFS is HTNV (Hantaan virus), which is related to the Apodemus mouse-borne virus in Asia. Different types of viruses have different hosts [4]. These different types of genotypes such as SNV, ANDV, etc. All these viruses can lead to hantavirus but the viruses have different might have different hosts. For example, field mice could cause Hantaan virus; Rattus norvegicus could cause Seoul virus; red bank voles could cause Puumala virus; yellow-necked field mouse could cause Dobrava virus. Usually, the viruses will store in their urine, droppings, and saliva. Analysis of the first molecule by HTNV revealed that the genome of HTNV contains three negative-sense single-stranded RNAs that share 3'-terminal sequences in the three genome segments. RNA genomes range in size from 11,845 nucleotides (nt) for HTNV to 12,317 nt for SNV. For all species of Bunyaviridae, each genomic RNA typically forms a circular molecule that passes through the reverse complements of the 3' and 5' ends of the linear viral RNA. The formation of base pairing occurs between this circular molecule. Hantavirus through viral glycoprotein adheres to host cell surface receptors that infect endothelial cells, epithelial cells, macrophages, follicular dendritic cells, and lymphocytes. There are three segments S (small), M (medium), and L (large) respectively, and encode the nucleoprotein (N), envelope glycoprotein (Gn, formerly G1, and Gc, formerly G2), and L protein or virus RNA (vRNA) dependent RNA polymerase (RdRp). Through the research, the result shows that bigger viral glycoproteins interact with the receptor which is integrin. From the investigation, the investigator found that the β1 integrin is a vole-transmitted hantavirus and is non-pathogenic. At the same time, β3 integrin is the main pathogenic hantavirus of HFPS and HPS and has multiple receptors [5].

2.2. Transmission, incubation period, and symptoms

Hantavirus is mainly transmitted through rodent urine, saliva, feces, and aerosols and always happened in rural regions which are closer to forests, and farms. Typically, in these places, there are more rodents here so there are more hosts that could spread the virus to people. These rodents always appear in barns, sheds, outbuildings, and houses. The people who work in these places has the potential crisis, they are the high-risk population [6]. Patients may experience headaches, dizziness, chills, fever, and myalgia, after that symptoms will be more severe including hypotension, acute shock, and acute renal failure these kinds of symptoms, which can lead to severe body fluid overload.

They also have a chance of developing gastrointestinal (GI) problems, which covered nausea, vomiting, abdominal pain, and diarrhea, after that patients will possibly suddenly arise from respiratory distress and low blood pressure. HPS has a long-time incubation period, symptoms usually first appear from 2 to 4 weeks after initial exposure, but symptoms may appear 1 to 8 weeks after exposure. For instance, nephropathy epidemical (NE) is a milder mutation from HFRS, and NE is mainly characterized by headache, back pain, abdominal pain, and fever, followed by subconjunctival hemorrhage, rash, and a less fortunate 1% may develop serious neurological problems or even epilepsy for about 3-4 days. Some patients are asymptomatic infections and others will have serious to the kidney. In the Americas, we have not found that hantavirus can be transmitted from person to person, but, in Argentina and Chile, some cases of ANDV that can be transmitted from human to human have been found, even if the number of cases is small, but it does appear. And some recent surveillance data have shown the presence of Puumala virus (PUUV) RNA in patient saliva. Nevertheless, there are inhibitors in the saliva, and these inhibitors may reduce the spread of the virus, thus achieving the goal of blocking [5].

3. Analysis of the cases of Hantavirus in the United States

3.1. Conclude the cases of Hantavirus in the United States

In the United States, investigators began to monitor the hantavirus in 1993 because at that time there was a very serious outbreak of respiratory disease at the border of the United States, and in 1995, the Disease Surveillance System (NNDSS) reported an existing patient in the laboratory with fever. Until 2015, the United States began to report some cases, but these cases did not show some cardio-pulmonary function symptoms, by 2015, some cases began to be reported, including attacks on cardiopulmonary function. From 1993 to the end of 2022, in the aggregate, there are 833 cases of hantavirus infection were reported in the United States, including non-pulmonary hantavirus infection and HPS infection. For a total of 158 cases from 1993 to 1999, investigators used questionnaires to ask relatives of patients to supplement the data already available. Having this data allows for easier monitoring, which is very specific and can give us a better understanding of the patient's journey before the illness, and even some activities at home. Through these questionnaires, investigators' investigations and reported rodent exposure locations classified possible locations into three categories: the patients' homes, workplaces, and their recreational areas. The case also considers whether the rodents are exposed to locations that are not easily noticed, such as in cars. In the case, patients were also divided into two categories, one is some activities that may be in direct or indirect contact with rodents (including work, life, entertainment, and people who often engage in outdoor activities), and the other unlikely exposure to rodent activity (mainly indoors). The occupations of these people are then carefully divided and further explored. From 1993 to 2015, through the analysis from CDC, the institutions reported that there are a total of 662 patients with laboratory-confirmed HPS cases. Of the 651 known cases in the laboratory, 230 (35%) died; mortality was also related to the region. Of these, 648 cases recorded information about their race. Most of the patients were white, not many Indians but they all lived in America. It can be seen from the report that Indians living in the Americas have a higher case fatality rate than white cases and are younger than whites. Most of the cases are in people aged 18 to 39 and people aged 40-64. The number of people affected is higher in the United States, and most of them are male. Of the known reports, it was concluded that 319 people had been exposed to rodents. In the western and eastern United States, rodents appear frequently, especially in the western United States, most patients have seen rodents in various places, or where rodents are likely to be present. Through these more than 600 cases, we have also identified some high-risk occupational groups. The establishment of early surveillance allows us to determine the cause of Hantavirus infection. Of course, we also found that HPS is more likely to appear in herdsmen, but only herders working in the U.S. Four Corners are at a relatively greater risk of exposure. Through research, that is believed that due to the environment of the Four Corners area, the Four Corners area is more likely to be exposed and receive more possibility of infection, and in

fact, the cases of HPS are very few cases only about 40 cases each year in America. In the United States, A total of 833 cases through 2020, 807 were HPS cases, and 26 were asymptomatic patients, most patients were male, accounting for 62 percent, while the remaining 38 percent are women. As mentioned earlier, hantavirus is more likely to appear in white people, white patients account for 73% of the total patients, 17% are American Indians and Alaska natives, and the rest 1% of Americans are black, 1 % are Asian, less than one percent is native Hawaiian, and the final 7% are unknown. From 5-year-old to 84-year-old patients, whose average age was 37.5, the mortality rate was around 35 percent, and in the Mississippi River in the west, the number of cases was as high as 94 percent [7].

3.2. To summarize the advantages and disadvantages and the analysis of the cases.

Epidemic monitoring early is a very effective way to control the epidemic. Although no exact statistics are showing that epidemic monitor can reduce the number of patients but epidemic monitoring makes people more familiar with the hantavirus and targets more accurate groups. Every year the number of patients decreases compare to before and more people notice hantavirus. Through surveys, we learn more about our audience. The method of WHO is to strengthen surveillance and active case detection, and follow-up with the people who have contact with patients. Monitoring is accurate. The information obtained from the family members of the patients has made the investigation of the epidemic more detailed. Although there is a certain amount of monitoring, it is temporarily impossible to fundamentally eradicate the impact of the hantavirus on our lives. The benefit of surveillance is that high-risk groups are identified from surveys [8].

3.3. Measures were taken during the epidemic

WHO has a method that is good for people to reduce the possibility of infection. More publicity, and let people know and understand this virus, reduce the chance of people getting sick, and tell people to get timely treatment. For those engaged in outdoor activities, pay attention to protective measures to reduce exposure to rodents and their excrement, mainly to reduce rodents.

4. Treatment of the virus

There are various treatment options for the hantavirus, such as antiviral drugs, immunotherapy, and vaccine development. In the drug, there is a variety of options, such as ribavirin, and favipiravir. Both drugs inhibit the expression of the virus. Ribavirin is an antiviral drug. The function of the drug itself is to rapidly enter phosphorylation after the drug enters the virus-cell, so that the product acts as a competitive inhibitor, blocking and inhibiting the expression of proteins and further inhibiting the virus copy itself. Favipiravir is a novel RNA polymerase inhibitor that selectively inhibits RNA polymerase associated with viral replication. The host cell can phosphorylate favipiravir to produce biologically active favipiravir-ribofuranosyl-5'-triphosphate (F-RTP), the viral RNA There will be a case of identification error, and the F-RTP will be wrongly identified. F-RTP inserts into the structure of the virus's RNA, thereby preventing RNA transcription and replication. In recent years, Favipiravir can deal with a variety of viruses, such as arenavirus, bunya virus, etc., and its drug properties are anti-influenza virus. Although favipiravir has been found to inhibit HTNV replication through experiments and observations, it has not yet been able to treat HFRS. There are three types of immunotherapy and vaccines. Immunotherapy is neutralizing therapy. However, the current research on neutralizing antibodies and immune serum is only limited to animal experiments, and there is no report on the clinical application of neutralizing antibody passive immunotherapy in HFRS.

Vaccines are divided into inactivated virus vaccines, viral vector recombinant vaccines, virus-like particle vaccines, and DNA nucleic acid molecule vaccines [9,10]. Inactivated vaccines have a short shelf life, and in clinical trials, less than 50% of vaccinated people are still effective 1 year after vaccination. Inactivated virus vaccines, currently available in both China and South Korea, are available in the market and vaccinated, mainly inactivated by formalin or β-propiolactone. As an alternative to inactivated vaccines, viral vector recombinant vaccines are recombinant vaccines based

on Gn and Gc recombinant vesicular stomatitis virus (VSV) or adenovirus (ADV) expressing hantavirus as a vector [11]. This method opens up a new direction for the study of the hantavirus. According to the existing research reports, the virus-like particle vaccine has been proven to be used. The S and M segments contained in the hantavirus genome or the expression products of the genes with the M segment can be assembled into a virus particle structure. And the particles of hantavirus under the electron microscope are similar, which also indicates that this vaccine may protect patients with HTNV infection for a long time. The other is a DNA nucleic acid molecular vaccine, which uses the immune response of T cells to penetrate CD4+ T cells. This is a nucleic acid molecule encoded by HTNV envelope glycoprotein Gc and lysosomal associated membrane protein 1 (LAMP1). The immune response time of mice is more than 6 months. For the mice injected for the first time, the mice will not be infected with HTNV within 4 months, so this vaccine has a crucial discovery for future vaccine development and protection.

5. How to prevent the next outbreak

When the next breakout carries out is unknown. No one knows when the next outbreak will be. People should keep away from rodents. For high-risk groups, protective measures can be worn when working. When collecting rodent body fluids, handle them properly to reduce the possibility of others being infected, prevent the next outbreak, and more importantly, people's cooperation to increase credibility and reduce non-cooperation. If there is a patient, quarantine as soon as possible, even if we are not sure if there will be human-to-human transmission, and tell people to watch out for rodents, be vigilant, and professionally treat. Improve customs testing, identify high-risk groups, and prevent the epidemic from spreading to other countries. In countries with vaccines, high-risk groups can be vaccinated. Even if the effective period is short and the protection rate is not high, it still has a certain protective effect.

Overall, people will have a deeper understanding of the hantavirus in the monitoring and investigation of the United States. From the analysis of mortality, infection rate, and other aspects, it is more convenient for investigators to target the target as soon as possible. During the investigation, the investigators also high-risk groups are more clearly defined, including age, gender, occupation, and other aspects. The overall summary of the type, development history, structure, and treatment of Hantavirus has also greatly enhanced epidemic prevention and control. In terms of fundamental prevention and control, people have adopted a variety of methods, such as controlling high-risk groups, quarantining common vaccines, keeping away from hosts, increasing awareness, increasing recognition, and increasing trust between people. These are crucial to preventing outbreaks and letting people be cautious and treat rodents with care, because the virus may be lurking inside, and popular science is also an important part of preventing and controlling outbreaks.

6. Conclusions

In general, the epidemic poses a great safety hazard to human beings, and irregular infections and outbreaks have also brought great inconvenience to people's lives. In the United States, whites are the high-risk group, and most will be infected with HPS, with an average age of around 37.5 years. Not only in the United States, but in fact, outbreaks occur in different regions almost every year. The Four Corners of the United States are high-risk areas in the United States, and Asian countries such as China and South Korea also have a great risk of transmission. And there is currently no vaccine certified by WHO, and the road to the vaccine is still long. For high-risk groups, vaccines can be considered but vaccines are not necessary. At present, we have not fully spread the knowledge of the epidemic to people, especially those in risk areas. We should speed up the development of vaccines, and develop more effective and long-lasting vaccines from existing vaccines and known drugs, to reduce people's concerns and promote human health. and researchers, to reach a consensus between risk groups and researchers.

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