Review Article

Hemorrhagic Fever history, Diagnosis and Treatment: review article

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ABSTRACT

Hemorrhagic fever viruses are risks to public health around the world because they can cause very deadly diseases to emerge and reappear. The viruses causing viral hemorrhagic fevers (VHFs) typically produce acute febrile illness, coagulation problems, and widespread bleeding, which can lead to potentially fatal organ failure. Four virus families are responsible for viral hemorrhagic fever (VHF), one of which is Filoviridae. The Filoviridae family includes the Ebola virus , is responsible for the current VHF outbreak in West Africa. Viral hemorrhagic fevers (VHFs) occur in various regions around the world, yet traditional diagnostic testing for these diseases has typically been conducted in major reference laboratories located in Europe and the United States. In this review, we explore the current understanding of the mechanisms driving the pathogenesis of viral hemorrhagic fevers (VHFs) and examine the progress in developing preventive and therapeutic strategies for these infections.

Keyword: Hemorrhagic Fever, Diagnosis , VHF, Viruses.

NTRODUCTION

Viral hemorrhagic fever (VHF) in humans can be caused by highly contagious RNA viruses called hemorrhagic fever viruses (HFVs). The most commonly symptoms of VHFs are mild to acute febrile disease, coagulation problems, and widespread bleeding that can result in multiple organ failure, and even death. Because of the emergence and reemergence of extremely deadly diseases that can cause life-threatening organ dysfunction, it poses a hazard to global public health. The mechanisms behind the viral pathogenicity linked to multiple organ dysfunction syndrome are currently poorly understood (1). Wild rodents, which often appear healthy, serve

as hosts for various pathogens. In these status humans are inadvertent hosts. While some of these viruses are recognized to be harmful to people. others are only recognized to be a cause of disease in a small number of clinical cases, which can sometimes begin with a single case that subsequently spreads to close contacts. Furthermore, numerous other arena viruses that are poorly understood are present in wild rodents, and there may be additional causes of viral hemorrhagic fever that are not yet discovered (2).

Clinical presentation and pathogenesis

The pathophysiological effects of viral hemorrhagic fevers (VHFs) led to their distinctive clinical manifestations. Generally, VHFs present with a consistent range of symptoms, predominantly characterized by fever and bleeding may be less pronounced in some cases. More severe manifestations include symptoms such as hemorrhage in the vessels and coagulation abnormalities., and failure of many organ systems. Patients typically first experience fever, which often accompanies influenza-like symptoms such as malaise, fatigue, muscle aches, sore throat, red eyes, headache, nausea, and diarrhea. Initially, nonspecific symptoms may evolve into more distinct signs such as flushing of the face and Truncula, a maculopapular rash, ecchymoses, petechiae, and obvious hemorrhage, edema in dependent areas, and hypotension, which around the fifth day of the infection can develop into shock. There is currently a lack of a thorough understanding of the pathogenic processes of VHFs. However, it is known that dendritic cells, macrophages, monocytes, and other important viral target cells and vascular endothelial cells. Once these cells are infected, the virus can spread through lymphatics to other organs (4). Viral hemorrhagic fevers (VHFs) cause abnormal vascular regulation and damage. Although they share certain clinical features, the specific cells and organs they affect, in addition to the molecular processes behind their pathophysiology, differ depending on the causative agent. Despite these differences, all VHFs target cells involved in initiating the antiviral response, leading to a delayed immune response. This delay results in high levels of viremia and immunosuppression in VHF patients, which can progress to a serious condition resembling shock in which markers of inflammation play a significant role. VHFs are typically transmitted via exposure to the inhalation of polluted materials through arthropod vectors or animal reservoirs. However, for most viral hemorrhagic fever transmission, from person-to-person interactions can take place via contact with blood or other body fluids that are contaminated (5). Viral hemorrhagic fevers encompass diseases brought on by 23 enveloped RNA viruses that are

members of our groups of organisms: *Filoviridae*, *Hantaviridae*, *Flaviviridae*, *Bunyaviridae*, and *Arenaviridae.* These diseases range from relatively obscure, geographically localized infections like Omsk hemorrhagic fever and Kyasanur Forest disease, to widely known infections such as the West African Lassa fever. Some VHFs, such as Ebola hemorrhagic fever, cause" sporadic outbreaks, while others are neglected endemic diseases that significantly impact public health. Not every virus within each family cause viral hemorrhagic fever (VHF) For instance, the arena virus lymphocytic choriomeningitis virus does not lead to VHF. Similarly, not every patient affected by a VHF agent will develop the syndrome; for example, only about 1% of individuals containing the Rift Valley fever virus experience symptoms of hemorrhaging and death. RNA genomes and filamentous, encapsulated virions are characteristics of filo viruses, such as the Marburg and Ebola viruses. The discovery of Ebola occurred in 1976 because of concurrent outbreaks of fever sickness, shock, and bleeding in Sudan and former Zaire. The Ebola virus comes in five different species, each with a different level of virulence. Three of These species lead to human epidemics: Zaire Ebola virus was the previous name for the Ebola virus (EBOV), the Bundibugyo and Sudan viruses. EBOV causes the largest and ongoing outbreak, which also marked the first reported case of Ebola virus disease (EVD) in West Africa. In 1967, the Marburg virus (MARV) was initially identified in Marburg's African green monkeys, Germany, where it caused a fatal illness in handlers. Since its discovery, Marburg virus cases have been reported in Zimbabwe, Uganda, Angola, Kenya, and the Democratic Republic of the Congo. These filo viruses often lead to outbreaks with high mortality rates, typically traceable to an initial human or animal infection. Increasing information from serology and molecular methods suggests that these viruses are stored in fruit bats, and infection in humans is likely obtained by coming into contact with these bats' bodily fluids (7,8).

SIGN AND SYMPTOMS

At first, viral hemorrhagic fevers (VHFs) were categorized as a single entity because its share common signs and symptoms see (table 1). Patients frequently show signs of fever and general malaise, which can resemble the symptoms observed in other tropical illnesses such as malaria and typhoid. The rarity of VHFs, combined with their nonspecific symptoms, complicates diagnosis, even once the disease becomes severe. Accurately distinguishing VHFs from different tropics illnesses is crucial not only for implementing effective seclusion and infection control measures to prevent The distribution of the virus but also for the appropriate VHF management and any concurrent diseases.(9)

Table 1 : Symptoms and Indications of Commoner VHF

Disease	Signs and symptom
Ebola Virus Disease	fever , headache, myalgia, hemorrhage ,abdominal pain , vomiting diarrhea ,chest ,pain ,conjunctival injection , fatigue, weakness
Marburg Virus Disease	fever,chills , headache ,myalgia hemorrhage, abcominal pain vomiting, nausea ,diarrhea ,chest pain, maculopapular rash jaundice
Lassa Fever	Fever, headache , myalgia, bleeding ,abdominal pain vomiting,nausea retrosternal chest pain, maculopapular rash, conjunctival injection enlarged cervical sore throat , lymphnodes.
Crimean-Congo Hemorrhagic Fever	fever , headache , back pain, bleeding ,abdominal pain , vomiting petechial rash, Jaundice, conjunctival injection photophobla , facial flushing , sore throat.

Spread of infection

Individuals spread viral hemorrhagic fevers by coming in close touch with bodily secretions from an infected individual, including blood, urine, feces, or saliva, or by touching mucosal membranes. Severely patients, those with higher viral loads are more likely to transmit the virus. After death, skin and skin structures can become heavily contaminated and may pose a risk of infection during burial practices. Secondary attack rates among close household contacts range from 3% to 17%. In healthcare settings, injuries from needlesticks are a highly effective mode of transmission for infections and are linked to higher mortality rates. There is neither epidemiological nor scientific data supporting airborne transmission of filo viruses. Sexual transmission from convalescent cases is possible because the virus can persist in semen for an extended period, but it is generally considered a relatively minor mode of transmission (10).

DIAGNOSIS

Viral hemorrhagic fever presents with no indications, which makes it challenging to diagnose early. challenging to differentiate them from other diseases like malaria and typhoid fever, as well as from one VHF causative agent to another. Compounding this difficulty the fact that VHFs often share similar laboratory parameters adds to the difficulty in distinguishing between

them. Additionally, the diagnostic value of serology is limited when the disease is at its most severe due to impaired antigen-presenting cells (APCs) and lymphocyte functions. This contributes to delays in diagnosis, even once the disease has progressed to a severe stage. (11). Given these challenges, detecting the viral genome is a more effective diagnostic tool for VHFs. However, blood sampling, which is necessary for this type of diagnosis, requires trained medical personnel and poses significant risks to both patients and healthcare workers. As a result, traditional diagnostic methods have been largely confined to important reference facilities in the US and Europe, limiting access to diagnostic services in endemic regions(12).Leukopenia, thrombocytopenia, and transaminitis (with aspartate transaminase [AST] levels higher than alanine transaminase [ALT]) suggest a possible VHF diagnosis in a patient with a relevant clinical history and credible epidemiological exposure within the past 21 days, especially if malaria tests are negative. New guidance from the Advisory Committee on Dangerous Pathogens (ACDP) recommends that these investigations be carried out urgently at local laboratories that standard precautions, along with additional splash precautions if needed, are followed, performing these tests is considered safe. Viremia begins on the first day fever which continues for the entire duration of the disease. IgM antibodies typically appear about the third day., while IgG antibodies usually develop by seven day; however, delays in antibody production can indicate a poorer prognosis. Therefore, non-invasive sampling methods, such as using saliva or urine, could be a worthwhile substitute. Right now, advancements in laboratory diagnostics are underway, includes lateral flow tests, multiplex PCR, and non-invasive sample techniques such collecting urine and saliva (13).

TREATMENT

Early diagnosis and supportive therapy are crucial for managing VHFs effective(including restoring fluids and treating problems related to electrolytes and coagulation), and management of secondary infections are crucial for improving outcomes in VHF cases. For Lassa fever, If ribavirin is given within the first seven days of fever, it has been demonstrated to lower mortality. However, its effectiveness in treating Crimean-Congo hemorrhagic fever (CCHF) is ineffective against filo virus infections and has unknown side effects (14). In models using non-human primates, investigational therapy, including three neutralizing monoclonal antibodies that target an EBOV protein has demonstrated some efficacy. Recently, this treatment was used in a sympathetic manner for seven examples of infected humans, of which five individuals survived (15). Two main factors must be given regard in the treatment of viral hemorrhagic fevers (VHFs): particular antiviral medication and life support to avoid multiple organ failure. Treatment should be tailored to the phase of the VHF: incubation, pre coagulopathy, and

coagulopathy. During the incubation phase, the most effective approaches include post-exposure, active or passive (16). Early diagnosis is crucial for the proper management of patients suspected of having viral hemorrhagic fever to increase survival rates and avoid nosocomial infections. Patients presenting with symptoms, or a history of travel indicative of VHF should be isolated. Healthcare employees providing care for these individuals must use appropriate personal protective equipment, known as VHF isolation precautions. While research into treatment options is ongoing, current management primarily relies on supportive care. For Lassa virus infections, ribavirin has been demonstrated to enhance the results of treatment when administered early on in the illness's progression. Still, research on its efficacy has been limited (17) more recent agents Currently being investigated are LASV-specific monoclonal antibodies and favipiravir as treatments for Lassa fever. At present, there are no effective vaccines available for Lassa fever. For hemorrhagic fever of the Crimean-Congo, treatment primarily remains supportive, Ribavirin has shown antiviral effects against Crimean-Congo hemorrhagic fever virus in vitro (18). Currently, effective human vaccines are not available. Workers in agriculture as well as those handling animals are advised to use insect repellent and refrain from touching blood or other bodily fluids from potentially infected animals or humans virus disease and Marburg hemorrhagic fever are primarily managed with supportive treatment. As of the now, there are no vaccines accessible for the Marburg virus(19). However, The Food and Drug Administration is one entity (FDA)-approved vaccine for Ebola, specifically targeting the Zaire ebolavirus. There are presently no proven antiviral therapies for dengue fever, there are currently no effective antiviral treatment fever, so management focuses on supportive care. While although there is just one vaccine especially in Southeast Asia and Latin America, the World Health Organization only advises people who have previously contracted dengue to get it (20).

Conclusion

Hemorrhagic fever represents a diverse group of severe viral infections characterized by high morbidity and mortality rates. Diseases such as Ebola, Dengue, and Lassa fever cause bleeding disorders and multi-organ dysfunction, which often make clinical management complex and challenging. Effective prevention and control rely on a multifaceted approach, including rigorous surveillance, prompt diagnosis, supportive care, and the development of vaccines and treatments. Continued research and global cooperation are crucial in combating these life-threatening diseases and mitigating their impact on affected populations.

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CONFLICTS OF INTEREST

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