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Key features of Ebola hemorrhagic fever: a review

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ABSTRACT

The current outbreak of Ebola virus in West Africa has become a devastating problem, with a mortality rate around 51%; over 3 132 deaths have been confirmed and even more are expected in this case. The virus causes a characteristic disease known as hemorrhagic fever. Its symptoms range from nonspecific signs such as fever, to more specific problems such as serious bleeding. Transmission occurs easily when a person comes in contact with contaminated fluids. Treatment is supportive because there are still no specific drugs for use. The present review focuses on the main features related to the Ebola virus, its transmission, pathogenesis, treatment and control forms. There is little in-depth knowledge about this disease, but its severity requires attention and information to prevent a worse scenario than the current.

1. Introduction

The recent outbreak of Ebola virus (EBOV) infection in Africa affects many countries, such as Guinea, Liberia, Sierra Leone, Nigeria, Senegal and Democratic Republic of the Congo and has not ceased. It is considered as the largest outbreak of EBOV disease ever recorded and is presently having devastating effects in West Africa. So far, this has already resulted in the deaths of >3 132 individuals associated with >6 643 recorded cases, with a mortality rate of approximately 51%[1,2], and there are estimates of occurrence of >20 000 cases in the next nine months[3].

EBOV is a highly pathogenic virus that has caused an increasing number of outbreaks in central Africa in the past decade and currently in West Africa. Due to its high fatality rate, it is very important to understand the mechanisms of pathogenesis and transmission to run an effective control and surveillance and to develop appropriate vaccines and therapeutics[4].

Ebola is Filoviridae, composed of a small group of non-segmented negative-strand RNA viruses, belonging to the order Mononegavirales. Filoviridae consists of one genus, filovirus, which contains two species: Ebola virus and Marburg virus, morphologically identical but serologically different[5].

EBOV hemorrhagic fever is a zoonotic disease that can be transmitted accidentally by direct contact with infected live or dead animals. Several researchers have attempted to unravel the natural history of EBOV in Africa since the first recorded human outbreak in 1976, along the Ebola River in Democratic Republic of Congo and Sudan. This can be defined as different ways in which this virus circulates in its natural environment, from its natural host to susceptible intermediate animal species (which worsen fatal infection), and then to humans, either via the natural host or through intermediate species (Figure 1)[6-8].

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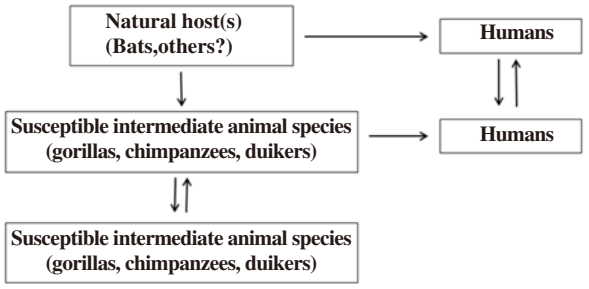

Figure 1. Natural history of Ebola virus.

2. Transmission

About the mechanisms of Ebola virus transmission in nature, it is known that once humans become infected, subsequent EBOV transmission continue to occur person-to-person mainly as a result of close contact with secretions, blood or tissues from patients. But how Ebola virus is originally passed to humans, nonhuman primates and/or other susceptible animal species, and what other factors might be involved in this transmission remains unclear yet[7].

Some animal species, as great apes and apparently duiker, are naturally infected by the virus, probably directly from a natural reservoir. These intermediate animal species develop a disease, which is often fatal. These infected animals thus spread the virus to other ecological niches linked to their environment and behaviors. After the death, their carcasses remain infectious for humans, who transmit the disease through community. Identification of the natural life cycle and determination of the virus reservoir should help in the development of strategies for preventing or controlling human outbreaks[8].

It is possible that humans can be directly infected by (unknown) EBOV reservoir species. Fruit bats of the Pteropodidae family are considered as the natural host of the Ebola virus. Bats seem to be involved with the first people to be infected during the 1976 and 1979 outbreaking in Nzara, Sudan. No other likely source of infection was identified in either outbreak. Added to this fact, an Australian who was infected by Marburg virus in Johannesburg, in 1975, had just returned from a trip to Zimbabwe, during which attended a site inhabited by many bats[8,9].

Ebola is not airborne, nor foodborne or waterborne. The initial human-to-human transmission must occur through contact with the body fluids of an infected patient. The EBOV does not infect other individuals during the the period between the initial infection and the onset of symptoms (incubation period), which can be 2-21 d[9].

It is believed that Ebola virus infection is transmitted through contact with body fluids or blood from infected monkeys or patients. Similarly certain family members became infected when caring for Ebola patients. How the infection enters the body remains unclear. The most likely route of infection is through contact of contaminated fingers with the conjunctiva or oral mucosa. Another characteristic is that the virus also can persist in convalescent patients. The finding of EBOV in body fluids of convalescent patients suggests that transmission may occur even during convalescence. But it is not clear how such patients can contribute to transmission[10,11].

Through the study in the families of 34 cases in Nzara in 1979, airborne transmission seems unlikely, showing the absence of risk due to simple cohabitation in the same room[5]. But transmission through aerosolized particles or vomit cannot be excluded completely, though it is believed that the major mode of transmission is through direct contact[11]. Because aerial transmission is of concern in the case of filovirus infections, the possibility of airborne transmission via animal-to-human and human-to-human transmission still needs to be known[12].

Due to the systemic nature of the infection in humans, it seems likely that a mammalian reservoir host is infected not only across the surface of the body, but also through the mucous membranes of the respiratory and intestinal tracts, for then a hematogenous spread occur along with subsequent infection of the tissues and organs and finally bleeding[13].

3. Pathogenesis

The key events that lead to shock and death are the impaired protective immunological responses, disseminated intravascular coagulation and increase in vascular permeability[6]. The model for EBOV pathogenesis is that, after entering the host, EBOV targets macrophages and dendritic cells, inducing an inflammatory state with high levels of proinflammatory cytokines. Simultaneously, the virus evades an immune response by some mechanisms including depletion of natural killer cells and lymphocytes and impairment of dendritic cells function. With infection of macrophages, they become activated and produce proinflammatory cytokines and tissue factor, thus provoking a pro-coagulant state. This state impairs endothelial barrier

function and develops into disseminated intravascular coagulation. Together, these events can lead to severe shock and death[4].

Virus induced shock has been associated with abnormal production of nitric oxide which is related to the loss of vascular integrity[14]. Shock syndrome can also have a contribution of platelet-derived agents triggered by damaged endothelial cells. Thus, gross damage of other organs can inducing thrombi formation in multiple organs and also cause disseminated intravascular coagulation in multiple organs[15].

4. Clinical features

After an incubation period that ranges from 2 to 21 d, infected individuals appear fever, chills, and malaise. An often early clinical sign is a conjunctival infection. Then occurs symptoms such as anorexia, vomiting, prostration, chest pain, and shortness of breath develop. A valuable differential diagnostic feature that may occur is the maculopapular rash related with erythema. In the prime of the disease, vascular dysfunction occurs as petechiae, ecchymoses, melena, menorrhagia, bleeding at needle puncture sites, presence of blood in the urine or faeces, mucosal bleeding and diffuse coagulopathy[4,6,11].

Between Day 6 and 16 may develop shock, multiorgan failure and coma with death due to vascular dysfunction[6]. Death is preceded by the appearance of hypotension, tachypnea, tachycardia and anuria[5]. A common consequence of infection is abortion, and newborns of mothers who die of infection are fatally infected. Convalescence is slow and marked by weight loss and prostration[13].

5. Diagnosis

The suspicion of Ebola hemorrhagic fever is based on clinical manifestations and on a history of contact with an infected person[11]. Laboratory diagnosis can be performed based on the detection of virus particles, particle components or virus specific antibodies[6]. But a method of practical and safe diagnosis would be helpful in Ebola outbreaks. In 1995, a diagnosis of Ebola hemorrhagic fever was difficult to confirm patient diagnosis in Kikwit, Democratic Republic of the Congo, due to lack of a safe and simple-to-use field diagnostic test[16].

6. Treatment

Currently, the treatment of Ebola hemorrhagic fever is no specific, but is mainly symptomatic and supportive. The proper intensive care treatment should be directed towards pain reduction, maintenance of electrolyte balance and effective blood volume[6,11,14].

Despite the absence of any specific antiviral drugs for the treatment of disease, inhibiting overexpression of tissue factor has been considered as a therapeutic approach, due to it has a profound effect in the development of disseminated intravascular coagulation[4].

Some drug candidates for treatment of Ebola hemorrhagic fever, such as estrogen receptor modulators, interferon, neutralizing monoclonal antibodies, rNAPc2 or siRNA, when administered shortly after infection, has shown protection, but do not have a therapeutic benefit after 2 d post infection. Another drug, pyrazinecarboxamide derivative T-705 (favipiravir), has demonstrated effectiveness against EBOV *in vitro* and *in vivo* (in mice), which makes it a promising drug candidate for treatment of Ebola hemorrhagic fever. But human clinical trials are still needed. This demonstrates that the investment in research to develop an effective antiviral therapy for human use is still necessary in this case[17].

7. Control and prevention

The control of Ebola virus infection has been further complicated due to the rapid progression of this disease. Decontamination plays an important role in preventing the spread of this infection because it is highly contagious[18,19]. Some control actions are recommended, such as early diagnosis with patient isolation, barrier nursing procedures, use of personal protective equipment by doctors, nurses, and caretakers, adherence to biosafety guidelines in laboratories and disinfection of contaminated areas and objects, and safe burials[14,20].

For the prevention of outbreaks of Ebola hemorrhagic fever, local people should avoid contacting with potential virus hosts such as bats, great apes or other susceptible animal species because evidence suggests that human filovirus infection directly come from these animals[7].

8. Conclusion

Currently, strict quarantine and symptomatic therapy are

considered suitable to prevent transmission of EBOV disease. But it can be seen that this is not enough, since the outbreak in West Africa has persisted and amplified over the past ten months. This can be because the outbreak spread to other countries, and inadequate medical system and traditional funeral proceedings in Africa that mourners often physically touch the body of the deceased[9].

The main obstacles in reducing the virus transmission is lack of knowledge and potential panic over the disease. The local residents of Sadialu village in Sierra Leone, which were infected with EBOV, refused to be hospitalized. There were rumours saying that the interventions to administer patients actually caused the disease[21].

The population of West Africa which includes people living in poor conditions and below the poverty line, turns out to be very susceptible to infection by EBOV. Such population is often overlooked by government and depends on the action of many volunteers who are willing to help them. This current outbreak of EBOV makes the precarious situation of inhabitants in West Africa more visible, waiting for an effective help for restoring and maintaining their health.

Conflict of interest statement

I declare that I have no conflict of interest.

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