Ebola – the most serious health challenge of modern times

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Abstract

The Ebola virus of the Filoviridae family causes haemorrhagic fever in humans called Ebola virus disease (EVD) or Ebola haemorrhagic fever (EHF). According to its places of occurrence, five subtypes of disease have been distinguished. EVD is transmitted by blood or other body fluids. In its initial stage, the disease is similar to influenza; in the final stage, patients manifest multiple organ failure, which leads to death. The mortality rate in EVD is up to 90%. In August 2014, the outbreak of EVD epidemic was declared in West Africa; moreover, the case of transmission of the disease to Europe was demonstrated. Considering the above risk, it is essential to exercise great caution and provide education for the travelling population and health care workers.

Key words: Ebola, health risk, disease

Introduction

An infection with Ebola virus of African origin causes an extremely severe Ebola virus disease (EVD) in humans. There are 5 species of Ebola viruses: Tai Bundibugyo Ebola virus, Sudan Ebola virus, Zaire Ebola virus, Reston Ebola virus and Las Ebola virus [1]. The ongoing epidemic of EVD in West Africa is caused by Zaire Ebola virus. On August 26th 2014, an outbreak of EVD epidemic was declared in the Democratic Republic of Congo; however, it is pointed out that both epidemics do not have the same sources [2].

The World Health Organisation (WHO) obligated seven countries to monitor and notify the infections, i.e. Guinea, Nigeria, Liberia, Sierra Leone, Senegal, USA and Spain. From December 2013 to October 12th 2014, 8 997 cases of EVD were registered, including 4 493 deaths. Moreover, on October 14th the first infection of a health care worker was found in the United States (Texas) [3]. In Madrid, a nurse who took care of a missionary was infected with Ebola virus. Health care workers are at increased risk of infection. To date, 416 medical professionals were affected, and more than half of them died [4].

The EVD epidemic shocked the world due to possible transmission of the disease from the affected African countries to the other regions. The issue has never been considered so seriously [5]. In August 2014, WHO declared the Ebola epidemic

in West Africa a Public Health Emergency of International Concern (PHEIC). During the meeting of the WHO Crisis Committee on September 16th all countries were requested to strengthen their readiness to take action, particularly by preparing simulations and providing proper training for medical personnel [6].

Virus

Viruses from the Filoviridae family are divided into Ebola and Marburg viruses. Filoviruses are filament-like viruses with the genetic material in the form of single-stranded RNA. They can have the same diameter of 80nm yet different length even up to 1400 nm. RNA encodes 7 genes, i.e. nucleoprotein (NP), virion-associated protein VP35, VP40, glycoproteins (GP), VP30, VP24, and RNA-dependent RNA polymerases (L) [7].

Five species of Ebola virus have been distinguished: Zaire, Sudan, TaiForest, Reston and Bundibugyo. Their names are related to the place of occurrence of a particular virus. Sudan and Zaire species were detected in 1976. The Zaire species caused many large disease foci of the mortality exceeding 50%, sometimes even 90%. The Bundibugyo virus caused the outbreak of EVD of the mortality rate of about 30% during the epidemic in Uganda in 2007 [8,9].

In 1989, the Reston species was detected, whose infection is asymptomatic. In 1994, another species

from the Ivory Coast was identified, called TaiForest. The Bundibugyo Ebola was detected as the last one in 2007; beside Sudan and Zaire strains, this virus is responsible for EVD [7,8]. The TaiForest virus was indentified in one individual as a factor causing EVD [10]. The Sudan virus is characterized by the 50% mortality. The virus was the cause of high mortality due to EVD during two epidemics of 1970 and one epidemic of 2004 in Sudan as well as one epidemic of 2000 in Uganda [11,12].

Pathogenesis

There are several routes of Ebola transmission in humans. Infections can develop through direct contact with blood or various body fluids of affected individuals. The virus is present in blood, urine, secretions of sexual organs and sweat. Its presence has been demonstrated in sperm even 7 weeks after successful treatment of EVD [13].

The Ebola virus invades the human body through mucous membranes and is distributed in the skin or parenterally. The virus infects many types of cells, including monocytes, macrophages, fibroblasts, endothelial and epithelial cells, etc. The initial replication occurs in macrophages, monocytes and dendritic cells, through which the virus passes to the internal organs, e.g. the liver, spleen and lymph nodes [14,15]. The infected cells release various inflammatory cytokines, e.g. macrophage inflammatory protein (MIP)- α , MIP- β , or TNF- α , whose high level leads to vascular leak as it increases the endothelial permeability [16]. The cellular immune response is reduced [17]. The dendritic cells attacked by the virus do not produce the antigen for T lymphocytes and do not induce the inflammatory response. Mediated by VP35 and VP24, the virus interacts with INF- γ , which is capable of stimulating macrophages to secrete neopterin. Neopterin reduces the cellular immune response. Its high level evidences a high risk of death [18]. Moreover, researchers claim that some undefined virus-host interaction plays an important role in the pathomechanism. Endothelial damage, apoptosis of lymphocytes, necrosis of the liver and adrenal glands impair the endothelial integrity and the immune system of the host [19]. The infected cells do not undergo apoptosis. It is believed that necrosis of hepatic cells is caused by decreased blood coagulation [14]. Furthermore, infection and necrosis of adrenal cells reduce the synthesis of hormones, resulting in shocks developing during EVD [7].

The EVD mortality is associated with high levels of proinflammatory cytokines and a high titre of the virus. The survival in EVD depends on the nucleoprotein (NP) response to the virus and activation of cytotoxic lymphocytes [16].

Symptoms and diagnosis

The mean incubation period of Ebola virus is 2-21 days; yet there are also cases of the 25-day incubation period. The first symptoms of EVD are similar to those in influenza. In many cases, the first symptoms are confused with malaria, shigellosis, cholera, colitis, typhoid fever, rickettsiosis or sepsis [20]. The patients affected have chills, fever, muscle and joint pains. The infection can also cause gastrointestinal disorders, e.g. nausea, abdominal pain, and impaired appetite. After about a week, the characteristic skin changes (central rash) occur, which change into haemorrhagic, maculopapular lesions after about 24 hours. EVD also attacks the respiratory system inducing sore throat and cough. The nervous system infection causes headaches, confusion; moreover, hyperagitation or fatigue and even coma are observed. Damaged cell membranes and impaired integrity of vascular walls lead to haemorrhages from the respiratory system (haemoptysis) and the gastrointestinal system (bloody vomiting and nosebleeds). In general, the patient diagnosed with EVD dies within one week after infection. In rare cases, patients recover 14 days after the first symptoms have developed [20,21]. EVD-associated deaths are caused by increasingly low arterial pressure and tissue necrosis due to multiple organ dysfunction syndrome (MODS) [22].

Diagnosis of EVD is based on meticulous history taking and is confirmed by clinical examinations of the material collected (isolation of the virus) [23]. Health care workers have to follow suitable safety measures during sampling due to a high risk of infection. After rendering the samples, the material is tested [7].

There are numerous methods for Ebola virus detection. The most effective of them is the detection of viral nucleic acid in the clinical material using reverse transcriptase PCR (RT-PCR) [24]. The RT-PCR test determines the virus subtypes. The method detects viral RNA in blood cells. Its positive results are confirmed by the enzyme-linked immunosorbent assay (ELISA) in about 80% [24,25].

ELISA enables the detection of viral antigens in blood of the infected and cured individuals. The

test is characterized by high sensitivity and is relatively easy to perform. Three types of ELISA are distinguished, which detect viral antigens, anti-EBOV IgG and IgM antibodies [26,27]

A less sensitive method is indirect immunofluorescence antibody test (IFAT) detecting anti-EBOV IgG in blood of the affected individual. The IFAT sensitivity can be reduced when the immune response is absent in severe EVD cases [27].

The radioimmunoprecipitation assay (RIPA) detects anti-EBOV antibodies. Moreover, Western Blot is used, which confirms the results of the tests performed earlier [27].

EVD epidemiology

In Europe, the first filoviruses were found in 1967 among individuals working in direct contact with animals, especially infected monkeys from Uganda. They caused extremely severe diseases, leading to an epidemic. The first EVD epidemic occurred in 1976 in Sudan and Zaire (the Democratic Republic of Congo). The pathogen of almost 90% mortality was isolated from the patient's blood and was called the Ebola virus (the river in the Democratic Republic of Congo [5]). The foci of disease occurred only in Sub-Saharan Africa; during the period of 90 years, the incidence of epidemic has been increasingly high [28]. The first case of EVD was found in Sudan in 1976 (po-wrózenie??). EVD is the disease of the highest mortality reaching 90% [29]. According to WHO, there were 8 994 cases of EVD between December 2013 and October 12 2014, including 4 492 deaths. Until mid-October 2014, 1 472 cases and 843 deaths were reported in Guinea, 4249 cases and 2458 deaths in Liberia, 3252 cases and 1183 deaths in Sierra Leone [30,31].

The WHO stressed extremely intensive transmission of EVD in Guinea, Liberia and Sierra Leone [30]. The evolution of outbreak is constantly observed in the above countries [32]. Official statistics are underestimated, especially in Liberia [32]. In Guinea, the incidence of EVD is increasingly high and new cases are reported in Beyla and Lola by the Ivory Coast. The most active regions of transmission are found in Freetown in Sierra Leone [30].

The fact of EVD transmission to Europe is alarming. At the beginning of October 2014, EVD was diagnosed in a health care worker in Spain. The worker took care of an infected patient, who was

transported to Spain on September 22nd and died three days later. This was the first case of EVD transmission outside Africa[33].

Treatment and prevention

Patients with EVD are administered supportive treatment, involving mainly broad-spectrum antibiotics. Intravenous fluids and electrolytes are supplied and supplemented. Shocks and haemorrhagic diathesis are countered. It is essential to maintain proper levels of oxygen and blood pressure in order to improve functioning of the cardiovascular and respiratory system. When patients develop additional infections, they are appropriately treated[5].

Prevention of disease transmission is crucial; patients should be isolated and barrier nursing procedures performed. Moreover, since the virus can be transmitted from cadavers, it is recommended to cremate bodies or bury them in hermetically-closed coffins. The use of individual safety and disinfection measures is of key importance [5]. The European Centre for Disease Prevention and Control prepared several guidelines, which reduce the potential risk of EVD infection. Above all, contacts with symptomatic patients, their body fluids and individuals who died due to EVD should be avoided. Another rule to follow is to avoid contact with wild African animals, both living and dead; their meat should not be consumed. Moreover, antiseptic rules should be definitely observed [34].

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