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REVIEW ARTICLE

Ebola Hemorrhagic Fever as a Public Health Emergency of International Concern; a Review Article

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Abstract

Ebola hemorrhagic fever (EHF) was first reported in 1976 with two concurrent outbreaks of acute viral hemorrhagic fever centered in Yambuku (near the Ebola river), Democratic Republic of Congo, and in Nzara, Sudan. The current outbreak of the Ebola virus was started by reporting the first case in March 2014 in the forest regions of southeastern Guinea. Due to infection rates raising over 13,000% within a 6-month period, Ebola is now considered as a global public health emergency and on August 8th, 2014 the World Health Organization (WHO) declared the epidemic to be a Public Health Emergency of International Concern. With more than 5000 involved cases and nearly 3000 deaths, this event has turned into the largest and most dangerous Ebola virus outbreak in the world. Based on the above-mentioned, the present article aimed to review the virologic characteristics, transmission, clinical manifestation, diagnosis, treatment, and prevention of Ebola virus disease.

Key words: Hemorrhagic fever, Ebola; health; emergency responders; virology; infection control

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Introduction:

Ebola hemorrhagic fever (EHF) was first reported in 1976 with two concurrent outbreaks of acute viral hemorrhagic fever centered in Yambuku (near the Ebola River), Democratic Republic of Congo, and also in Nzara, Sudan. There have been almost 20 other outbreaks that involve nearly 2500 cases happened before 2014. With the exception of a single case identified in the Republic of Ivory Coast in the 1990s, all of them were reported in sub-Saharan Africa involving the Sudan, Gabon, Uganda, and Democratic Republic of Congo (1). But the current outbreak (2014), which is the largest one ever documented, is the first recorded outbreak of Ebola in West Africa (2). The previous largest outbreaks of Ebola virus was identified in Uganda in 2000–2001, which was caused by Sudan Ebola virus (SUDV) subtype. This outbreak resulted in nearly 400 cases, 216 of which were laboratory confirmed and had 53% overall case-fatality rate (3). The 25th known outbreak of the Ebola Virus was started by reporting the first case in March 2014 in the forest regions of southeastern Guinea. Its infection rates reached 13,000% within a 6-month period. In August 8, 2014 the World Health Organization (WHO) declared the epidemic to be a Public Health Emergency of International Concern (2, 4). Thereafter, Ebola virus has spread through the West Africa and appeared in Senegal, Sierra Leone, Liberia, Nigeria, and now it has been reported in Spain and United States of America, too. With more than 5000 involved cases and nearly 3000 deaths, this event has turned into the largest and most dangerous Ebola virus outbreak all around the world (5). Based on the above-mentioned, the present article aimed to review the virologic characteristics, transmission, clinical manifestation, diagnosis, treatment, and prevention of Ebola virus disease.

Virologic characteristics

Ebola virus is a lipid-enveloped ribonucleic acid (RNA) virus, which belongs to the Flavivirus family and known since 1976. It consists of five different sub-types and Ebola virus Zaire sub-type (ZEBOV) was the first one to be recognized in the Democratic Republic of Congo. The current Ebola virus has 97% homology with ZEBOV (6, 7). Other subtypes include Bundibugyo (BDBV), SUDV, Côte d'Ivoire or Tai Forest (TAFV) and Reston Ebola viruses (RESTV). Ebola hemorrhagic fever (EHF), caused by ZEBOV, has the highest fatality (57%–90%), followed

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by SUDV (41%–65%) and BDBV (40%) and these 3 subtypes are responsible for the large outbreaks that recently occurred in Africa. However to date, RESTV infection has been observed in animals in Asia and as an asymptomatic disease in humans, while TAFV has only been identified in 2 human cases, both of which were nonfatal (4, 8, 9).

Transmission

Some authors claimed that a 44-year-old man suffering from malaria was the first identified fatal case of EHF who was infected using a contaminated needle for administration of parenteral chloroquine in the Democratic Republic of Congo (previously named Zaire) in 1976 (1). On the other hand, some researches indicated that the first person became infected through contact with an infected animal (4). Fruit bats that live in Guinea and its neighboring countries are considered as the natural hosts of Ebola viruses, and other mammals serve as accidental hosts. This virus has been implicated as one of the major causes of decreasing African chimpanzee and gorilla populations in recent decades (1, 10, 11). Ebola is one of the zoonotic viruses that can lead to a highly fatal disease in human beings. Humans are also one of the accidental hosts and can be infected through close contact with blood and bodily fluids of another infected case (including humans and animals), either by direct contact or indirectly from a contaminated environment. It seems that mosquitoes and other insects do not play a role in virus transmission and also it is not spread through the air (1, 4, 10). Ebola virus has high transmissibility and virulence and less than 10 viral particles are enough for becoming infected. The incubation period range is 2-21 days (average 5-6). Fortunately, the disease is not transmissible until the patient becomes symptomatic, but it continues to be contagious, even postmortem (2, 12). Family and healthcare providers caring for Ebola patients are at the highest risk for becoming infected because of their possible contact with contaminated blood or body fluids. So the virus can easily spread if reasonable preventive precautions are not taken (4).

Clinical Manifestation

The patients with suggestive symptoms, including unexplained hemorrhage and risk factors within the last 3 weeks such as contact with suspected or confirmed EHF cases, or travel to an endemic area should be evaluated for EHF (2). EHF is a fatal disease (mortality rate 50%-70%) that can occur 2-21 days after exposure to the virus. The initial clinical presentation is non-specific. Early clinical symptoms of EHF include abrupt onset of fever, fatigue, myalgia and headache followed by progressive gastrointestinal symptoms such as anorexia, nausea, and abdominal discomfort accompanied by vomiting and diarrhea within 1-2 days. This process can lead to intravascular volume depletion and also profound electrolyte disorders, hypoperfusion, shock, and multi-organ failure (acute respiratory, liver, and renal failure) within a few days. The "hemorrhage" in the phrase "Ebola hemorrhagic fever" is a late manifestation, which usually occurs as gastrointestinal bleeding, conjunctival hemorrhage, epistaxis, and hemorrhagic rash. Some others believe that these symptoms occur only in a minority of patients, that is why they use "Ebola virus disease" instead (1, 2, 5, 9, 10, 12-16). Complete blood count usually shows leucopenia and thrombocytopenia, but hemoglobin levels almost never decrease significantly. Intravascular volume depletion and hypoperfusion are manifested by metabolic lactic acidosis and renal insufficiency. Massive diarrhea associates with profound hypokalemia and hematogenous spread of virus to the liver and spleen and leads to hepatocellular injury marked by elevated liver enzymes (2, 5, 12-14). Analysis of coagulation profile shows increased prothrombin and partial thromboplastin times (PT and PTT) accompanied by detection of fibrin degradation products in the occurrence of disseminated intravascular coagulation (DIC) (6).

Diagnosis

Apart from Ebola virus, there are other types of viruses that can cause hemorrhagic fever, including Crimean-Congo hemorrhagic fever virus, Marburg virus, Lassa virus, and emerging ones such as Lujo virus. These viruses have particular public health importance because of their spreading ability to healthcare workers, difficulties in their rapid recognition, lack of effective specific therapeutics, and high fatality rate (10). Definite diagnosis of a clinically suspected case of Ebola virus infection requires laboratory confirmation. In EHF, viremia develops after the fever and takes up to 3 days to confirm the diagnosis by proper laboratory evaluation. It is necessary to collect serum, plasma, or whole blood samples of at least 4 milliliters, and take them to the appropriate health department, refrigerated or on ice, for further testing. Early diagnosis is confirmed via detecting viral antigens by using polymerase chain reaction (PCR) or enzyme-linked immunosorbent assay (ELISA) on the blood sample. Later in the disease course, antibodies against the virus such as Immunoglobulin M (IgM) and Immunoglobulin G (IgG) can also be detected. If the test results were positive, local and state health departments should be notified immediately. However, because of the extreme biohazard risk, using antigen- or antibody-based assays or PCR testing should be performed in level 4 biosafety laboratories, which is more possible in developed countries where such laboratories are available (1, 2, 17). Centers of Disease Control and Prevention (CDC) have performed standardized enzyme-linked immunosorbent assay (ELISA) for detection of Ebola virus specific antibodies. This test has high sensitivity and can be used for detecting antibodies in human beings even 10 years after exposure to the virus (6).

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Treatment

There is no specific antiviral agent or vaccine against Ebola viruses. Therefore, supportive care is the most important aspect of its management. Aggressive prevention of intravascular volume depletion is critical to avoid life-threatening complications by using proper fluid therapy, oxygen therapy, correcting profound electrolyte abnormalities, and preventing the complications of shock such as acid–base derangements. Treatment of other infections, if they occur, and close monitoring of vital signs and regular biochemical and blood gas checks should be done. These proceedings are considered as the foundation of critical care medicine and should be applied to both resource-rich and resource-constrained settings. With improving supportive cares, EHF outcomes may also improve. Symptom control with taking narcotics and benzodiazepines were often reported as the end-of-life therapy in some patients (2, 5, 14). A variety of chemotherapeutic agents have been tested for different stages of development. Recombinant human activated protein C and recombinant nematode anticoagulant protein C_2 are also among them. One drug identified as ZMAPP, has been used on several patients, however it remains unclear if it is effective or not. Therefore, no Food and Drug Administration (FDA) approved agent exists against Ebola (4, 6, 18-23). Figure 1 shows the latest CDC algorithm regarding emergency department evaluation and management for possible Ebola infected patients.

Prevention

The current outbreak of EHF highlighted the importance of prevention strategies. Health care workers have represented a considerable proportion of all infected cases. So educating and training the medical staff on universal precautions, risk assessment, and use of personal protective equipment is crucial. Patients initially identified as having a possible viral hemorrhagic fever should be isolated until the results of their specific diagnosis are obtained from reference laboratories. It is important not to delay diagnosis and treatment of more common diseases, such as malaria or typhoid, during this period. Follow-up of contact cases is essential for infection containment in case the patient tests are positive. Specially equipped ambulances and trained staff should be prepared to do the transferring when needed (1, 10, 24). Early diagnosis and rapid laboratory confirmation along with isolation of patients and following their contacts, as well as access to protective equipment and environmental decontamination are the mainstay of prevention.

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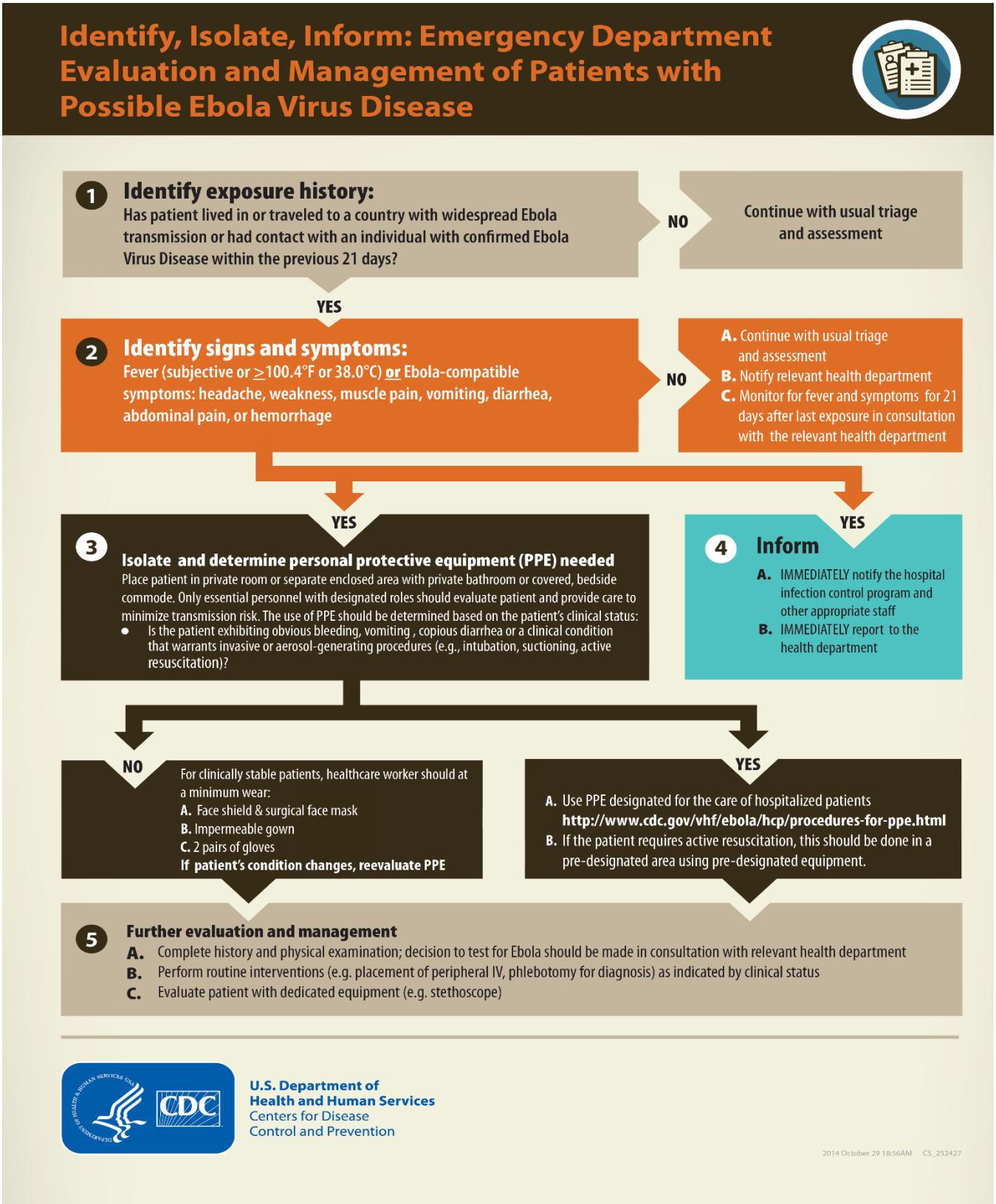

Figure 1: Shows the latest CDC algorithm regarding emergency department evaluation and management for possible Ebola infected patients.

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