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Ebola Virus Disease

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Definition:

Ebola virus is named after the river in the former Zaire where a haemorrhagic fever initially identified in 1976 involved human to human transmission, as well as spread by contaminated injection equipments [1]. Ebola virus causes an acute febrile illness associated with a high mortality rate. The illness is characterized by multi-system involvement that begins with abrupt onset of headache, myalgia, fever and proceeds to prostration, rash, shock and bleeding manifestation.

Epidemics usually begin with a single case acquired from an unknown reservoir (bats suspected) and spread mainly through close contact with sick persons or their body fluids either at home or in the hospital.

Etiology

The family filoviridae comprises two antigenically and genetically distinct genera Marburg virus and Ebola virus. Ebola virus has five readily distinguishable species named for their original sites of recognition: Zaire, Sudan, Cote d'Ivoire, Buno Bugyo and Reston [1].

Ebola virions

Typical Filovirus particles contain single, linear negative sense single standard RNA arranged in a helical nucleocapsid. Virions are 790-970nm in length. They may appear elongated or contorted forms. These viruses are destroyed by heat (60° in 30 minutes) and by acidity but may persist for weeks in blood at room temperature [1].

Epidemiology

Ebola virus first appeared in 1976 causing severe hemorrhagic fever in Zaire and Sudan (550 cases).

Mortality was 90% and 50% respectively. Both epidemics were associated with inter human spread.

After 20 years, Zaire Ebola virus recurred in the Democratic Republic of Congo in 1995 (317 cases) and in smaller epidemics in Gabon in 1994-1996 mortality rate was 88%.

Deep forest exposure again resulted in an epidemic in Gabon in 1994 - 2003.

Present episode

Mainly five countries in West Africa - (Guinea, Liberia, Nigeria, Senegal, and Sierra Leone) have been affected. This epidemic began in Guinea during December 2013. WHO was officially notified of the rapidly evolving EVD outbreak on March 23, 2014. On August 8, the WHO declared the epidemic to be a "public health emergency of international concern". As of September 14, 2014, a total of 4507 confirmed and probable cases of Ebola virus disease have been detected. 2296 deaths from the virus, have been reported and the case fatality rate is 50 %.

Clinical features

Patients in the age group 15 to 44 years have been involved, with an incubation period 2 to 21 days. Principal manifestations are fever, fatigue, headache, arthralgia, myalgia, abdominal pain and chest pain. Dyspnoea, sore throat, diarrhoea and loss of appetite, bleeding from puncture sites and mucus membranes, petechiae, echymosis, pupura and finally death is due to multi-organ dysfunction syndrome (MODS) and septic shock can ensue [1-4].

Pathology and pathogenesis

Ebola and Marburg viruses replicate virtually in all cell types including endothelial cells, macrophages and parenchymal cells of multiple organs [2].

The earliest involvement is the mononuclear macrophage system and that is responsible for initiation of the disease process. In human disease and Macaque models upregulation of tissue factor and disseminated intravascular coagulation are the inciting mechanisms.

Viral replication is associated with cellular necrosis both in vivo and vitro. In light microscopy level, the changes are liver necrosis with councilman bodies, intracellular inclusions of viral nucleocapsids, interstitial pneumonitis, cerebral glial nodules and small infarcts. Antigen and virions are abundant in fibroblasts and Interstitium. The appendages of subcutaneous tissues also contain virions and antigen and they escape through small breaks in the skin or possibly through sweat glands also. Hence close contact with patients and touching of the diseased may be avoided. Inflammatory cells are not prominent even in necrotic areas.

Virus interacts intimately with cellular cytokine system. There is high level of pro inflammatory cytokines which contributes to the severity of illness.

Virus is resistant to the antiviral effects of interferon. Viral infection of endothelial cells selectively inhibits the expression of major histocompatibility complex class I molecules and blocks the induction of several genes by the interferons. In addition glycoprotein expression inhibits and α V integrin expression and that leads to detachment and subsequent death of endothelial cells in vitro and that correlates with the limited inflammatory response evident in lesions.

How to categorize and confirm Ebola virus disease (WHO definitions)

Suspected case: Is any person alive or dead, who has (or had) sudden onset of high fever and had contact with a person with a suspected, probable or confirmed Ebola case or with a dead or sick

animal OR

Any person with sudden onset of high fever and at least 3 of the following symptoms, headache, vomiting, anorexia, diarrhoea, lethargy, myalgia, arthralgia, dysphagia, dyspnoea, or any person who had unexpected bleeding or who died suddenly from an unexplained cause.

Probable case: Is any person suspected to have EVD who was evaluated by a clinician or any person who died from suspected Ebola and had an epidemiologic link to a person with a confirmed case but was not tested and did not have laboratory confirmation of the disease.

Confirmed case: A probable or suspected case is classified as confirmed when a sample from the person was positive for Ebola virus RNA, antigen or antibody.

Laboratory findings in Ebola virus disease

Important laboratory findings which can occur in Ebola virus disease are leukopenia, thrombocytopenia, hypoproteinemia, proteinuria, deranged coagulation profile due to disseminated intravascular coagulation (DIC), increased levels of SGOT, SGPT (mild) and increased serum amylase [3].

Differential Diagnosis

Differential diagnosis of Ebola virus disease include viral hemorrhagic fever (Dengue), Falciparum malaria, Leptospirosis, Rickettsial fever, Typhoid fever, Gram negative sepsis, Cholera and Shigellosis [2].

Diagnosis

Travel and work history along with exposure to wild life animal [1], isolating the virus by cell culture of blood, CSF or throat washings taken during the viremic phase of illness and from postmortem tissues in fatal cases, viral antigen by ELISA [2], detecting the viral RNA by RT-PCR of blood or other tissue fluids or gingival brushings [2], detecting IgM and IgG antibodies by ELISA in recovering patients [2] are important in diagnosis of Ebola virus disease. EBOLA eZY screen promoted by Vedalab, an European company may prove to be a rapid diagnostic kit for diagnosing Ebola virus disease in 15 minutes where monoclonal anti body is reacting to the presence of virus in a tiny sample of blood, plasma or urine. The test is yet to be marketed.

Treatment

No specific treatment [1] is available for Ebola virus disease. Supportive care in the form of intravenous fluids, antipyretics, vasopressors, oxygen, fresh frozen plasma and red cell transfusions are given as needed. Hemodialysis for renal failure, heparin for DIC, antibiotics to prevent secondary infections and activated protein C infusion have been used.

Convalescent phase plasma has little in vitro neutralizing capacity and is not protective in humans or in passive transfer experiments in monkeys and Guinea Pig models [5]. Studies in Rhesus monkeys have shown improved survival among animals treated with an inhibitor of Factor VIIa / tissue factor or with activated protein C.

Ebola virus disease developed in a patient who contracted the disease in Sierra Leone and was airlifted to an isolation facility in Hamburg, Germany, for treatment. During the course of the illness, he had numerous complications, including septicemia, respiratory failure, and

encephalopathy. Intensive supportive treatment consisting of high-volume fluid resuscitation (approximately 10 liters per day in the first 72 hours), broad-spectrum antibiotic therapy, and ventilatory support resulted in full recovery without the use of experimental therapies [6].

Prevention

Primary prevention: Public education [2]

Secondary prevention: Standard precautions for infection control, isolating the patient, quarantine and contact tracing (Senegal method) are used.

Ebola vaccine

Phase 1 Studies of cAd3 - EBOV have begun in the United States and the United Kingdom already. Researchers plan to begin enrollment for trials of rVSV soon. Both vaccine candidates have demonstrated 100% efficacy in non human primates but how that will translate to human subjects remains unknown [7,8].

Prognosis

Death usually occurs around the 9th day of illness secondary to hypovolumic shock and multi organ failure. The case fatality rate is lower for Ebola Sudan (50-60%) than for Zaire (78-90%). Even well resourced hospital settings have demonstrated a higher rate of mortality (80-90%) especially in Angola and the Democratic Republic of Congo for Ebola hemorrhagic fever [9].

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