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Ebola virus disease: Report from the task force on tropical diseases by the World Federation of Societies of Intensive and Critical Care Medicine

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ABSTRACT

Ebola virus is a filovirus that can cause fatal hemorrhagic fever (HF) and five distinct species exist that vary in terms of geographical distribution and virulence. Once the more virulent forms enter the human population, transmission occurs primarily through direct contact with infected body fluids and may result in significant outbreaks. The devastating has been the recent West African outbreak.

Clinically, signs and symptoms are similar to those of the other VHFs [4]. The incubation period is 2–21 days, followed by fever, headache, myalgia, diarrhoea, vomiting and dehydration; thereafter, there may be recovery or deterioration with collapse, neurological manifestations and bleeding, that can lead to a fatal outcome.

Elevated hepatic transaminases is common and severe hepatitis is more common in fatal cases and frequently there is associated fluid depletion. Real time reverse transcription-PCR (RT-PCR) techniques on blood specimens are the gold standard for diagnosis [6].

Management is discussed and is essentially supportive with strict attention to infection control and prevention. None of the pharmacological interventions have shown conclusive benefit and future management of epidemics should centre around prevention and containment, specifically isolation, hygiene, and vaccination.

Contents

1. Introduction

Ebola virus disease (EVD) and Marburg Virus Disease are categorised as filoviruses and can cause fatal hemorrhagic fever (HF) [1]. Five distinct species have been ascribed to the Ebolavirus genus, namely Zaire,

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Sudan, Taï Forest, Reston and Bundibudyo Ebola viruses [2]. These viruses vary enormously in terms of geographical distribution and in their virulence in humans, with Ebola Zaire one of the most lethal infections known to mankind. The recent West African outbreak was caused by a Zaire Ebola virus very similar to those that have caused previous outbreaks in the Democratic Republic of the Congo and Gabon [3].

The natural ecology of Ebola viruses remains largely obscure. Evidence hints that a specific arboreal species of bat may be the reservoir for the Zaire species [4], but the specific mechanism of transfer from bat to human or bat to other forest-dwelling animals is not known. However, various human outbreaks have been traced to contact with "bushmeat", including the slaughtering of chimpanzees and bats [5].

Once the virus enters the human population, transmission is primarily through direct contact with infected body fluids such as blood, faeces and vomitus. Owing to this mode of transmission, the virus has a propensity to spread in the hospital setting and between close contacts. The possibility of a viral HF should always be considered as delay in diagnosis increases the potential for mortality and transmission [6].

More than 20 outbreaks of EVD have been reported since 1976 [7]. Before 2014, these occurred in isolated settings with the largest involving 425 laboratory-confirmed cases reported from Gulu, Uganda, in 2000 and 2001 [8]. By April 13, 2016 however, after the World Health Organization (WHO) had declared the West African epidemic to be over, the disease had accounted for a total of 28,652 cases with 11,325 deaths. During this period >800 healthcare workers (HCW) inclusive of nurses and nurse aides (accounting for >50% of infections), doctors and medical students (12%), laboratory workers and trade and ancillary workers (janitors, maintenance staff, etc.) (7% each), contracted this disease with nearly 500 losing their lives [9]. Importantly although the majority of infections were confined to West Africa, EBV had been transmitted to 7 countries including Nigeria, Senegal, the USA, the United Kingdom, Italy and Spain [10]. On the 13 May 2017 another outbreak with 3 deaths was reported in a remote area of the Democratic Republic of Congo emphasising the an ongoing risk of future epidemics and potential for international spread [11].

As such, it is wise always to maintain a high index of suspicion, especially for patients presenting with a compatible clinical syndrome and who have histories that indicate a risk of having contracted an HF-causing virus such as travel to endemic regions or contact with animals, raw bushmeat or sick patients.

2. Clinical features

Clinically the signs and symptoms of EVD are not dissimilar to those of the other VHFs [12]. Following an incubation period of 2–21 days (mean 4–9 days), three phases occur; initially fever, headache, and myalgia, followed by diarrhoea, vomiting and dehydration; thereafter, in the second week, there may be recovery or deterioration with collapse, neurological manifestations and bleeding that can lead to a fatal outcome. The differential diagnosis of VHF is broad and may include many treatable infectious diseases, most notably malaria, bacteraemia (including meningococcemia), African tick bite fever, and even non-infectious conditions such as haematological malignancies, liver failure and heatstroke. In a report subsequent to the epidemic describing the clinical features in patients admitted to one hospital in Sierra Leone, the presenting features were compared with other infections presenting to the same hospital. No clinical feature was diagnostic, the odds ratio (OR) for the disease being EBV was calculated as follows; fever [OR: 1.2 (0.8–1.8)], vomiting [OR: 1.6 (1.1–2.1)], diarrhoea [OR: 1.5 (1.1–2.0)], intense fatigue [OR: 1.7 (1.2–2.4)], anorexia [1.1 (0.8–1.5)], abdominal pain [OR: 0.9 (0.6–1.2)], muscle pain [0.8 (0.6–1.1)], and joint pain [OR: 0.6 (0.4–0.9)] [13]. The bottom line is that diagnosis cannot be made by clinical features alone and prompt laboratory diagnosis is critical.

3. Laboratory diagnosis

Rapid diagnosis facilitates management and triage of suspected cases, the optimisation of infection prevention and control (IPC) and allocation of clinical resources, assists with surveillance and contact tracing and also determines when the patient can be discharged into the community [14].

The laboratory features are not diagnostic, however can narrow the differential and give an indication of prognosis. In a recent study [15] documenting the laboratory features of the disease abnormal liver function was common, with 70% of patients having elevated alanine transaminase (ALT) or aspartate transaminase (AST) >five times the upper limit of normal (ULN) [15]. Severe hepatitis (AST >15 times ULN) was more common in fatal cases (93% vs 44%) as was a higher mean haemoglobin concentration, haematocrit, and median platelet count, possibly indicating fluid depletion. Thrombocytopenia was more common in non-fatal cases with values of 146×10^9/L versus 197×10^9/L. Similarly, low median white cell count, lymphocyte count and granulocyte count predicted survival, with granulocytosis and lymphocytosis more common in fatal cases. Overall the strongest risk factors for mortality were RIFLE-3 acute kidney injury, severely raised AST, high haematocrit, low Ebola virus Real time reverse transcription-PCR (RT-PCR) cycle threshold, hyperkalaemia, C-reactive protein >100 mg/dL, and granulocytosis [15].

RT-PCR techniques on blood specimens have become the standard for diagnosis and RT-PCR performed on oral fluid is the standard for post-mortem testing [16,17].

Novel tests have reached the field, and these include automated nucleic acid amplification (NAATs) and rapid antigen detection tests. WHO guidance documents state that nucleic acid amplification tests are preferred when feasible and that rapid antigen detection tests should serve as "presumptive" or "screening" tests in remote settings without access to immediate molecular testing or to assist in triaging high-risk patients when caseloads are high [14,18,19].

4. Management

The sophistication with which these patients are treated will depend on the environment and on the facilities available [20]. One patient in 1996 was treated in an ICU in South Africa and in the recent epidemic 27 patients were managed in nine countries outside of West Africa, with a survival of 81.5%. The accounts of these patients have shown that intensive care management in a modern ICU is feasible [21,22].

Given the extremely high mortality rates and the highly infectious nature of VHFs, (infectious doses are as low as one viral particle for some), the haemorrhagic fever (HF)-causing viruses have to be handled and stored in the highest biosafety- and security-level laboratory conditions, and patient management must adhere to stringent isolation and barrier nursing protocols.

During an epidemic or even between epidemics a case definition must be established. This heightens awareness and increases potential for early recognition [23]. Thereafter consideration must be given as to the design of the ICU to ensure that the possibility of infection is reduced. This has been well described previously [22,24]. Essentially, a large area with isolation rooms, a large antechamber for donning and doffing of protective clothing, and an observation area should be available. Dedicated diagnostic apparatus including X-ray, ultrasound and point-of-care laboratory equipment, infusion pumps, ventilators, and dialysis machines should be accessible within the area. Waste, including soiled linen (we use condemned linen which is incinerated post use) must be disposed of appropriately.

All Staff involved in the care of patients should be adequately trained and educated with well-defined roles. Multidisciplinary teams are necessary which include non-clinical staff such as administration, laboratory staff, cleaners, morticians and security [25].

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