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Ebola in West Africa: be aware and prepare

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Ebola virus disease

Ebola virus along with Marburg virus forms the family *Filoviridae*, which causes severe viral haemorrhagic fever in humans and non-human primates. Ebola virus causes Ebola virus disease (EVD), previously known as Ebola haemorrhagic fever [1] (Fig. 1). Since its discovery in 1976 until 2013 there were 24 recognized EVD outbreaks centred on central and west equatorial Africa totaling around 2,100 documented cases [2]. The natural reservoir is believed to be fruit bats [3]. The mode of transmission to humans is likely to be through bush meat, and then from human to human via direct contact with bodily secretions, particularly blood and gastrointestinal fluids (the virus can also be detected in saliva, semen, breast milk, and other fluids). The case fatality rate in previous outbreaks has approached 90 % [1, 4].

Current outbreak

The current epidemic started in December 2013 in Guinea [5] and has spread across land borders to Liberia and Sierra Leone, Nigeria, and most recently to Senegal. An unrelated outbreak has emerged in the Democratic Republic of Congo. By 22 August 2014 there were a total of 4,269 cases and 2,288 deaths. The current epidemic is unusual in terms of the number of people infected, number of health care workers, and spread of disease [6]. The explanations for this are complex, and are attributed to poor health infrastructure (following conflict and civil war), with few health care workers, poverty, and low educational level [7]. This has led to extreme fear causing denial of the disease, abuse of health care workers, avoidance of health care facilities by those who are sick, closure of health care facilities due to sick and scared staff, and overload of health care facilities that are open. There is a high level of health care worker infections. The case fatality rate stands at 53 % in the current outbreak; however, there may be many fatalities which have not been accounted for owing to cases hidden by communities/families [8].

Clinical presentation

Overall there are very few publications on clinical presentation and management of EVD, as the outbreaks mainly occur in patients in resource-limited settings where intensive/critical care is rarely available, and documentation is often challenging [9]. Emergency and critical health care workers practising in countries distant from the epidemic should be aware of the current outbreak, and should take a

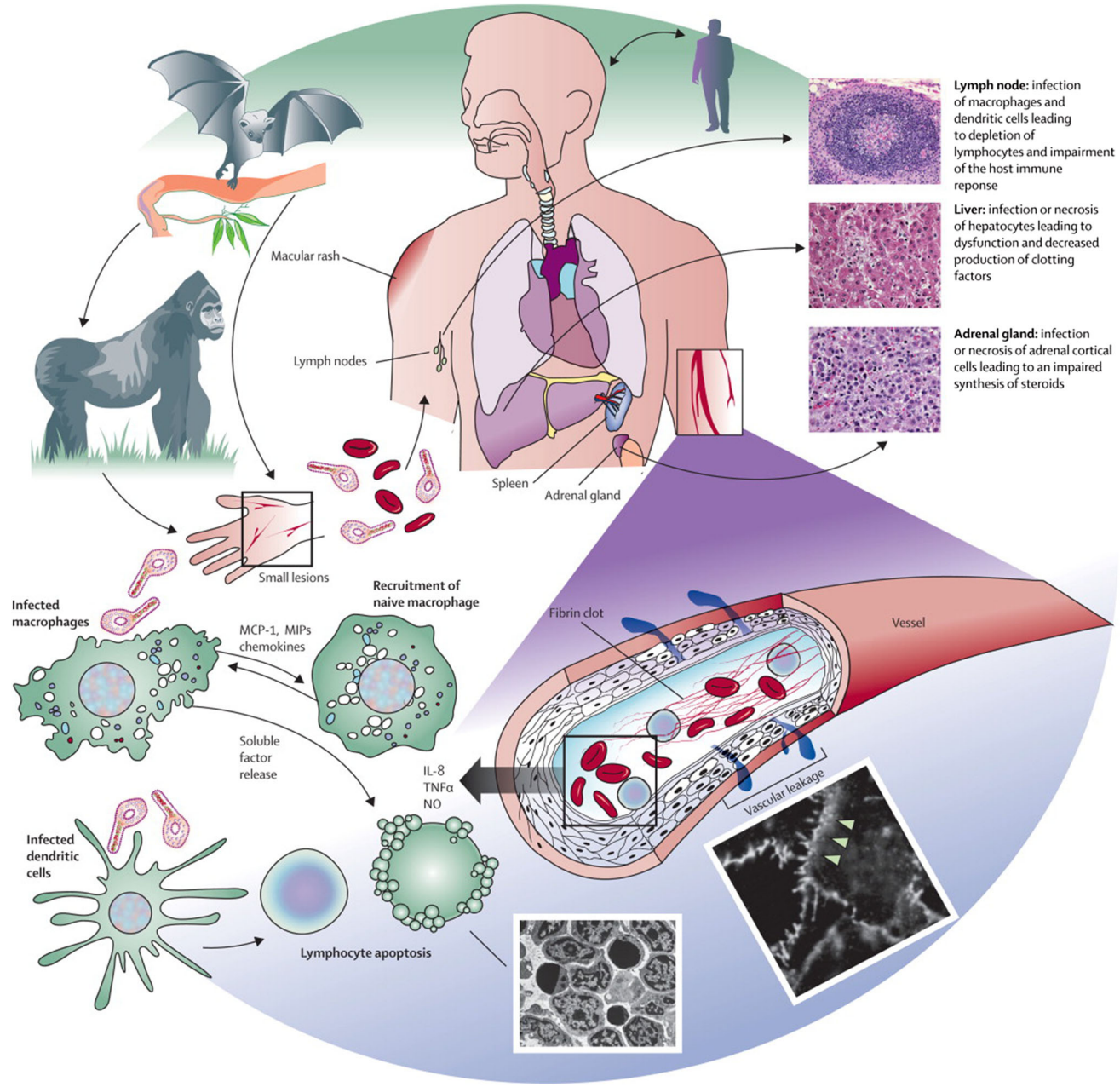

Fig. 1 Pathophysiology of Ebola haemorrhagic fever includes two critical points illustrated in this figure: (1) endothelial damage mediated by both the virus and the up-regulation of toxic cytokines, which leads to extensive vascular leakage, and (2) disseminated intravascular coagulation, which leads to severe thrombocytopenia. Figure originally published in [1]

careful travel history from anyone who is presenting with a febrile illness. Once travel to or residence in an affected area within the last 21 days is established, further careful epidemiological history is critical. Risks include contact with blood or other bodily fluids of a patient with known or suspected EVD, participating in funeral rites/burials in disease-endemic areas, and direct handling of bats, rodents, or primates from disease-endemic areas [10]. The assessment should include symptoms such as headache, muscle pain, vomiting, diarrhoea, abdominal pain, weakness, and signs such as fever, rash, conjunctival haemorrhage and bleeding.

How to manage an EVD suspect

Patients with a temperature (above 38.0 °C) and epidemiological risk factors should be isolated immediately

and staff should use personal protective equipment when dealing with a person under investigation (PUI) [10]. Standard, contact, and droplet precautions should be used [11]. The local national reference laboratory should be contacted before collection of any biological samples for advice on collection, management of waste, and transportation precautions. Local infection control teams should be alerted.

Diagnosis in the early disease (day 3–16) includes testing for viral antigen detection ELISA and for RT-PCR, or antibody IgM capture ELISA (after 2 days to at least 30 days); later in the disease or after recovery virus isolation direct ELISA for IgM and IgG (develop from day 6 onwards and persist for years) can be used [1]. The highest biosafety laboratory should be used to analyse samples (BSL-4). It is imperative to rule out other causes or co-infections causing fever in returning travelers.

The clinical course and severity are highly variable and the following information is taken from combined reports of Marburg virus disease (MVD) and EVD [12]. The patient temperature is often between 39 and 40 °C early in the course of EVD, but wide swings with drops below normal are possible. A relative bradycardia can occur in early disease with tachycardia (120–140 bpm) developing later. A rash develops in 25–52 % of cases, usually early in EVD, which is non-pruritic, erythematous, maculo-papular. It may progress to become diffuse, confluent, and generalized. Desquamation may occur in convalescence. Conjunctival haemorrhage is the most frequent sign of abnormal clotting, with bruising and bleeding (often at venepuncture sites) also common. Palpable lymphadenopathy, tender hepatomegaly, abdominal pain and tenderness, jaundice, and hiccups have all been reported.

Supportive investigations have been limited given the resource-limited settings of the outbreaks, but the following have been noted: progressively dropping haemoglobin, thrombocytopenia, and leukopenia (low lymphocytes, increased percentage of granulocytes). Later there may be increased leukocytes, but fatal cases often remain leukopenic. Liver function testing can reveal a high AST greater than ALT (mean AST more than seven times higher than ALT in fatal cases), alkaline phosphatase normal or high, gamma GT high, bilirubin can be normal or high. Adrenal insufficiency is a sequelae of EVD, but cortisol has been rarely performed. A low calcium (below 6 mg/dl) may be associated with fatal disease. Renal function may be normal, but a progressive decline is more common in fatal cases. Oliguria is possible and haematuria and proteinuria have been reported. Coagulation abnormalities include a prolonged PT, PTT, and bleeding time. Disseminated intravascular coagulation can occur in late disease, and can be the cause of death. D-Dimer may correlate with fatal cases.

Confirmed cases should be transferred to a national treatment centre if available. There has been no prospective evaluation of supportive therapies [13]. In many cases treated in African outbreaks patients received antimalarials and antibiotics. Acyclovir and ribavirin have been used on a few cases, but there is no evidence for efficacy. Oral rehydration was used preferentially over intravenous rehydration, in an attempt to reduce transmission risk. Blood products such as whole blood, packed cells, fresh frozen plasma and platelets have been utilized. Clotting factors and other regulators of coagulation have been employed in a small number of cases, as has heparin to prevent thrombosis and disseminated intravascular coagulation. On the ground, reports from West Africa suggest that mortality appears to be associated with overwhelming sepsis rather than haemorrhage; therefore, critical care management is vital.

Interventions

There is no proven intervention for EVD. Since the 1970s convalescent serum or blood has been utilized as a potential therapy. At least one of the US patients who survived received a transfusion from a convalescent patient. ZMapp which is a serum of three monoclonal antibodies has been used on five medical workers; so far two US citizens and a British nurse have survived, but a 75-year-old Spanish man has died, as has a Liberian doctor. TKM-Ebola is an RNA compound that binds to Ebola; phase 1 human trials are underway. Other broad-spectrum antiviral agents (favipiravir, BCX4430) may be useful but human trials have not been performed. An experimental vaccine developed in 2005 based on vesicular stomatitis virus was effective in macaques; it was used on a German laboratory care worker in 2009 who survived. The GSK/NIAID chimpanzee virus vaccine has shown responses in non-human primates [14]. There is an urgent ongoing discussion on testing these experimental products during this current epidemic.

Summary

This epidemic has been declared a Public Health Emergency of International Concern [6] and many countries have issued updated national guidelines on EVD [11, 15]. We urge health facilities to consult these and to develop local action plans [16]. During this epidemic the internet and social media such as Twitter are being effectively used to disseminate information by the WHO, governments, and the medical press. As the WHO is predicting that that the end of the epidemic is far away and it may infect up to 20,000 people before it is controlled, it is essential that the global medical community remains

informed and vigilant. We urge the critical care teams working with patients who have been evacuated to resource-rich settings during the current epidemic to share their best practices as soon as possible.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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