Short Communication

Experiences of Response Measures against the 4 Suspected Cases of Ebola Virus Disease from West Africa in the National Center for Global Health and Medicine, Tokyo, Japan

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SUMMARY: In Japan, infectious diseases are classified into 4 types based on how contagious and severe the pathogens are, and Ebola virus disease (EVD) is categorized as a category 1 infectious disease. The National Center for Global Health and Medicine in Tokyo, Japan, is designated as a specified hospital for category 1 infectious disease patients and has experienced 4 probable cases of EVD from West Africa. Even after the outbreak in West Africa is ended, we should continue to pay attention for new EVD outbreaks. Increasing the number of infectious disease specialists with the proper knowledge of viral hemorrhagic fever, including EVD, is a common problem for infectious disease physicians working in Japan, the academic society, and the government.

Ebola virus, which belongs to the genus *Ebolavirus*, family *Filoviridae*, is among the most virulent human pathogens (1). The Ebola virus disease (EVD) epidemic in West Africa resulted in more than 28,610 reported cases and more than 11,308 deaths through March 2016 (2). Although imported or medically evacuated cases have been reported in the United States and European countries (3), there have been no report of EVD cases in Asia, including Japan.

In Japan, infectious diseases are classified into 4 types based on how contagious and severe the pathogens are. EVD is categorized as a category 1 infectious disease along with other viral hemorrhagic fevers, plague, and smallpox (4). The Ministry of Health, Labour and Welfare (MHLW) and the local prefectures have designated specified infectious disease hospitals (specified hospitals) and class 1 infectious disease hospitals (class 1 hospitals), respectively, to provide treatment for category 1 infectious disease patients in an isolated biosafety ward at public expense.

The National Center for Global Health and Medicine (NCGM) is a tertiary care general hospital in Tokyo, Japan, with an isolated biosafety ward with 4 beds for specific and category 1 infectious diseases. The NCGM has been designated as a specified hospital, and 4 probable EVD cases from West Africa have been treated there. The aim of this study was to share our experiences of probable EVD cases for improving the coping strategy of medical institutes and public administration in Japan.

Four probable EVD cases between October 2014 and

March 2016 were seen at the Disease Control and Prevention Center, NCGM, Tokyo, Japan. Table 1 shows the summary of the 4 cases. During this period, a probable case was defined by the MHLW as i) history of travel to endemic countries within 21 days and fever or ii) history of contact with body fluids of patients and feeling of warmth (5).

According to the Infectious Disease Law in Japan, probable EVD cases are transferred from quarantine or a public health institute to an isolation room. Two infectious disease doctors (1 attending doctor and 1 fellow or resident) and 1 to 2 nurses are assigned a work shift with rotations every 8 hours. In our department for infectious diseases, there are 6 attending doctors, 2 fellows, and 2 residents. Three attending doctors and 3 fellows or residents are assigned to the EVD team and work in the biosafety ward for the whole day. The remaining doctors work in the outpatient and inpatient wards, covering the EVD team's duty. In addition, 22 nurses are assigned to care for emerging infectious disease patients and are trained every month. These doctors and nurses generally work in the general ward in the NCGM but are convened on the isolated biosafety ward of the NCGM when probable cases occur. The chief of the department of infectious diseases serves as a leader involved in the negotiation and coordination with executives of the

Table 1. The summary of 4 cases of probable EVD in the National Center for Global Health and Medicine, Japan from October 2014 to March 2016

Case	Date	Country	Ebola PCR	Duration of isolation (day)	Final diagnosis
40s M	2014/10/27	unknown	negative	3	unknown
60s M	2014/11/7	Liberia	negative	2	streptococcal pharyngitis
30s M	2014/12/29	Sierra Leone	negative	2	sinusitis
70s F	2015/1/18	Sierra Leone	negative	3	influenza A

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NCGM, MHLW, Tokyo Metropolitan Government, the local health department, the quarantine station, and the National Institute of Infectious Diseases, Japan, in addition to evaluating the case management. The deactivation of patient isolation is decided by the leader.

Figure 1 shows the personal protective equipment (PPE) used in the NCGM when we care for patients with category 1 infectious diseases, including EVD. All healthcare workers in the NCGM used the PPE shown in Fig. 1 during the management of the 4 probable cases discussed here. When we undertake invasive procedures such as tracheal intubation, we use a powered, air-purifying respirator instead of the face shield and N95 mask; however, there were no chances to use such a respirator for these 4 cases.

In the isolation room, a sphygmomanometer, thermometer, oxygen saturation monitor, and electrocardiographic monitor were arranged. We evaluated vital signs every work shift. When the patient was able to check his or her own vital signs, we received the information from the patient through a television-phone to minimize exposure. There is a mini laboratory room in the isolated biosafety ward of the NCGM equipped with machines for complete blood counts and biochemistry. Rapid diagnostic tests for malaria, dengue fever, influenza, and *Streptococcus pyogenes* are also available.

We experienced 4 probable EVD cases after November 27, 2014. On November 21, 2014, the MHLW announced a new definition, as described previously. Between August 2014 and September 2015, 9 probable EVD cases were noted in Japan (6). All 9 probable cases, including our 4 cases, were observed after the announcement of the new definition. Because we cannot know when a case of probable EVD or true EVD will emerge, physicians in specified or class 1 hospitals should construct, in advance, the framework of a team, a risk-management

strategy, and a chain of command in their institutes. With the decrease in the cases of EVD in West Africa, the MHLW changed the definition of probable EVD on September 18, 2015, to be i) fever $> 38^{\circ}\text{C}$ or clinical symptoms of EVD, and ii) history of contact with body fluids of EVD patients or history of contact with bats or primates in endemic countries within 21 days (7). Since that change, there have been no cases of probable EVD, and on January 14, 2016, the World Health Organization (WHO) declared the end of the EVD outbreak in West Africa (8).

Our department was divided into 2 groups. One group was the EVD team, consisting of 7 doctors (1 leader, 3 attending doctors, and 3 fellows or residents). Another group continued the daily work, including in the outpatient and inpatient wards. The work for each doctor increased much more than usual. Considering that a probable case of EVD can emerge suddenly and cannot be predicted, specified or class 1 hospitals must retain sufficient numbers of infectious disease specialists. In our cases, no patients were confirmed to have EVD, and the period of admission in the isolated room was 2 to 3 days. Our EVD team consisted of 7 medical doctors, which was likely sufficient for a probable EVD case. However, if EVD is confirmed, patient care could be more intensive and prolonged, from several weeks to several months. The team for a confirmed EVD case needs many more medical doctors to maintain the quality of care. Sufficient doctors should be assigned in the institutes for the care of confirmed EVD patients. According to the MHLW, there are only 443 doctors working as infectious disease experts in Japan (9). However, there are 28 specified or class 1 hospitals that retain them (10). Increasing the number of infectious disease specialists with the proper knowledge of viral hemorrhagic fever, including EVD, is a common problem for infectious disease physicians working in Japan, the academic society, and the government. The MHLW launched a program called the Infectious Disease Emergency Specialist Training Program in 2015 (11). This program aims to train infectious disease experts in epidemiology and risk management. The Japan International Cooperation Agency began taking applications for membership in the Japan Disaster Relief Infectious Disease Response Team to facilitate support in a wide range of areas relating to infection control measures (12), which will contribute to preparing physicians for managing clinical infectious diseases, especially for emerging and re-emerging infectious diseases.

Expertise beyond that of infectious disease physicians is needed for EVD patient care. In developed countries, EVD patients often need intensive care and resources such as ventilators and continuous hemodiafiltration (3,13). Emergency physicians, intensivists, and biomedical equipment technicians are expected to join the team for EVD patient care.

In case 1, we repeated the PCR test for the Ebola virus. The first negative result could not rule out EVD because the patient's blood sample was collected within 72 hours from the onset of symptoms (14). The final diagnosis was unknown, but we believe it was a benign disease because the patient's fever disappeared quickly and he did not relapse.

In all cases except for case 1, an alternative diagnosis

Fig. 1. Personal protective equipment (PPE) in NCGM for category 1 infectious diseases, including Ebola virus disease. It consists of a face shield, goggles, N95 mask, double gown, double gloves, shoe covers, and boots.

was made, such as streptococcal pharyngitis, acute sinusitis, or influenza A. The final diagnoses of the other 4 probable cases of EVD treated in Japan were malaria (6). If an alternative diagnosis is not made, it is difficult to determine when isolation of the case can be discontinued. The physicians who encounter patients with probable EVD need to be aware of not only emerging and re-emerging infectious diseases but also other general infectious diseases. Six of the 9 probable EVD cases were diagnosed as malaria, streptococcal pharyngitis, or influenza A, which could be diagnosed with commercially available rapid tests. Because body fluids such as blood and airway secretions of patients with probable EVD could be contagious, they should not be discharged from the biosafety ward without precaution. It is important to prepare rapid diagnostic tools in the biosafety ward in advance. After the outbreak of EVD in West Africa, we placed BioFire, a multiplex PCR machine, in the isolation room to detect a variety of pathogens, including Ebola virus, simultaneously within just an hour. Early detection of the pathogen will contribute to risk management and early treatment.

Person-to-person transmission of Ebola virus is associated with direct contact with the body fluids of individuals who are ill with EVD, or who have died from the infection, in the absence of PPE. There was 1 breakdown of PPE when we cared for these 4 cases. A nurse had touched her face with her gloved hand when she was taking them off in the anterior chamber. Healthcare workers are at increased risk for infection in outbreaks of EVD (15). Healthcare workers require regular practice in how to put on and remove PPE to prevent nosocomial transmission of Ebola virus.

Although the WHO declared the end of the outbreak, there are still sporadic cases in West Africa. Patients recovering from EVD continue to have infectious viruses in certain body fluids, such as semen, vaginal secretions, ocular fluid, and breast milk, even after the virus is no longer present in the blood (16,17). There has been 1 confirmed case of sexual transmission of the Ebola virus during the epidemic in West Africa, which demonstrated evidence of the persistence of infective Ebola virus in semen for 179 days or more after the onset of EVD (18). Sporadic cases of EVD may continue to be reported in West Africa; thus, healthcare workers must be permanently prepared for EVD. For example, standard precautions should be provided for all patients in all medical settings on a routine basis. The common practice of taking a travel history for febrile patients is also important for early detection. Cross-subsidization among medical institutions, such as dispatch of experts, is needed.

In conclusion, we shared our experiences of response measures against the 4 probable cases of EVD from West Africa in a specified infectious disease hospital in Japan. Even after the end of the outbreak in West Africa, we should be prepared for EVD.

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Conflict of interest None to declare.

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