Emerging Infectious Disease (2): Marburg Hemorrhagic Fever

Yung-Cheng Su, MD; Yuh-Jeng Yang, MD; Tzong-Luen Wang, MD, PhD

Abstract

Since its first identification in 1967, Marburg virus has been notorious in the recent 20 years because of its high mortality rates, and the capacity of dramatic outbreaks. The potential to spread the disease worldwide has become a reality with the expansion of global transportation and international trade. Physicians need to be aware of the potential danger of Marburg hemorrhagic fever, be able to identify the disease, and know how to manage and prevent its transmission.*(Ann Disaster Med. 2005;3 Suppl 2:S47-S51)*

Key words: Marburg Hemorrhagic Fever; Surveillance; Biological Event

Introduction

Marburg virus first identified after some laboratory workers in Marburg, Germany, developed hemorrhagic fever after contacting tissues from African green monkeys.[1-3] Although only few outbreaks were reported,[4-7] the high mortality rate once infected, the inability to identify the natural host and poor understanding of transmission make the diagnosis, management and prevention difficult.

Like Ebola virus, Marburg virus is considered to have potential to be used as biological weapons in terrorism because of high mortality rates, low virion counts needed for infection, relative stability, infective aerosol nature, and the possibility of person-to-person transmission.

Epidemiology

Marburg hemorrhagic fever was first recognized in 1967, when outbreaks occurred simultaneously in laboratories in Marburg and Frankfurt, Germany and in Belgrade, Serbia. The infected people included laboratory workers handling the tissues of the African green monkeys from Uganda, as well as several hospital staffs and family members caring for them.

No other case had been recorded thereafter until 1975, when a 20-year-old Australian traveler was admitted to a hospital in Johannesburg, South Africa. He might have been infected in Zimbabwe during his trip, and passed the virus to his traveling companion and a nurse. In 1980, a 56-year-old Frenchman became acutely ill after his trip form Western Kenya not far from the Uganda. Marburg hemorrhagic fever was identified, and the patient's attending physician became the second case.

From Department of Emergency Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
Address for reprints: Dr. Tzong-Luen Wang, Department of Emergency Medicine, Shin-Kong Wu Ho-Su Memorial Hospital, No 95, Wen Chang Road, Taipei, Taiwan
Received: Feb 5 2005. Revised: Feb 15 2005. Accepted: Mar 3 2005.
TEL: 886-2-28389425 FAX: 886-2-28353547 E-mail: M002183@ms.skh.org.tw

Another Marburg infection was recognized in 1987, when a 15-year old Danish boy who had traveled in Kenya, including western Kenya, became ill and died.

The first large outbreak in Durba, Democratic Republic of the Congo occurred from late 1998 to 2000. 154 people were involved, and 128 were fatal. The majority of victims were young male working in a gold mine. After the outbreak subsided, there were still some sporadic cases reported in the region.

Recent outbreak happened in October 2004 is believed to have begun in Uige Province, Angola. As of 20 April 2005, the Ministry of Health in Angola has reported 266 victims, of which 244 were fatal, representing the mortality rate more than 90%. This outbreak is the largest and on record for this disease by far.

Pathophysiology

Marburg virus can affect both humans and non-human primates. It is a unique zoonotic RNA virus of the filoviridae family, which is Latin words for "thread virus"; Ebola viruses are the only other known members of the family by far. The two diseases are almost clinically indistinguishable. Both are rare, have high mortality rates, and have the capacity of dramatic outbreaks. Filoviruses have the potential of being used as "Category A" biological weapons, because of the high lethality, ability to be aerosolized, and the ability to induce fear and anxiety. Unfortunately, the outbreaks seemed to alert the health authorities only after the transmission has been aggravated by inadequate disease control.

Although the native geographic area of Marburg virus is still in question, according to the past records, this endemic area appears to include at least parts of Uganda, Western Kenya, and perhaps Zimbabwe. Like Ebola virus, the actual animal reservoir remains a mystery, and how the animal host transmits Marburg virus to humans is unknown.

However, victims of Marburg hemorrhagic fever may spread the virus to other people. Spread of the virus between humans often occurred in a hospital, or in close contact. Direct contacts with body fluids, blood of the patients, or other objects contaminated with infectious tissues are all highly suspected as sources of transmission.

Clinical features

After an incubation period of 3 to 10 days, the onset of Marburg hemorrhagic fever is abrupt with fever, chills, severe frontal headache, and myalgia. Around the fifth day after the onset, maculopapular rashes, most on the trunk (chest, back, stomach), may occur, and followed by nausea, vomiting, diarrhea, abdominal pain, chest pain and sore throat. Rashes may be nonexistent, transient, nonspecific, or petechial. Hemorrhagic symptoms include epistaxis, hemoptysis, hematemesis, or gums bleeding.[8] Symptoms may become increasingly severe, include jaundice, pancreatic inflammation, weight loss, delirium, shock, liver failure, and multi-organ dysfunction. Death often occurs 6 to 9 days after the onset of the symptoms.

Recovery from the disease may be prolonged and accompanied by orchititis, hepatitis, transverse myelitis, uvetis or parotitis. Previous large outbreak in the Democratic Republic of Congo from 1998 through 2000, had a mortality rate of 83%. On the other hand, Ebola hemorrhagic fever has shown mortality rates differs from 53% to 88%, according to the dif-

ferent virus strains.

The possibility of person-to-person transmission is greatest during the latter stages of illness. Transmission during the incubation period has not been reported, but the patients may become infectious during the first few days since the onset of fever.[9]

Diagnostic Strategies

Marburg hemorrhagic fever should be considered in patients who had traveled to West Africa in the recent 3 weeks present with acute febrile illness without other apparent source. The diagnosis should also be suspected if patients have had direct contact with body fluids or blood of a person or animal with this disease in either the trip or during the work. The likelihood of acquiring Marburg hemorrhagic fever is extremely low in persons not meeting any of these criteria.[9]

Two factors make the rapid recognition of the outbreaks difficult: the extreme rarity and its similarity to other diseases. Many signs and symptoms of Marburg hemorrhagic fever are similar to those of other infectious diseases, makes the early diagnosis difficult and early suspicion important. Different diagnosis include dengue hemorrhagic fever, typhoid fever, malaria, leptospirosis, relapsing fever, meningococcemia, relapsing fever, rickettsial infections, viral hepatitis, the acute form of African trypanosomiasis, and other arboviral infections.[10]

The laboratory assessment of suspected patients should include a complete blood cell counts with differential, hepatic function testing, urinalysis, chemistries, blood cultures, and urine cultures. Leukopenia and thrombocytopenia may increase the likelihood of viral hemorrhagic fever, but these results are not specific. Blood cultures may help to diagnose bacterial infection, and peripheral blood smear may help to rule out malaria. Polymerase chain reaction (PCR), virus isolation, antigen-capture enzyme-linked immunosorbent assay (ELISA) testing and IgM-capture ELISA can be used to confirm the diagnosis within a few days after the onset of symptoms, but these examinations are not available worldwide. Confirmation of the disease is often made long after the emergency department visit.[10,11]

Management

Treatment for Marburg hemorrhagic fever is primarily supportive, including airway protection with ventilator support when necessary, adequate fluid supply, maintenance of electrolytes balance, and vasopressors for the hypotension. If the coagulopathy was developed, transfusion of fresh-frozen plasma and other blood products may be needed to replace the coagulating factors and platelets. Most patients need to be admitted to the intensive care unit for continuous monitoring and management. Ribavirin, which has been seemed effective in the treatment of Lassa fever, does not have good in-vitro activity for Marburg virus.[12, 13]

Prophylaxis

Owing to the limited knowledge of the disease and the absence of a vaccine, effective prevention against transmission from the original hosts has not yet been established. Preventions of secondary transmission are therefore the most important prophylaxis by far. Rapid identification the disease and isolation of patients is the first step to prevent the outbreak. Patients in

the hospital should be placed in negative-pressure isolation rooms to minimize the possibility of in-hospital spread and the need for transfer if the condition deteriorates. When caring patient with suspected or confirmed Marburg hemorrhagic fever, barrier nursing techniques should be used to prevent direct physical contact. These precautions include wearing of protective masks, gloves, and gowns, and proper disposal of patient excretions, needles, and equipments.

Since people who have close contact with patients are at risk, they should undergo daily medical surveillance by an appropriate infection control agency. These include the healthcare workers in the hospital. Isolation measures should be started immediately in any febrile patient who has traveled to the endemic area of Marburg hemorrhagic fever within 10 days before fever onset, has contacted with blood or other body fluids from a infected person or animal, or worked in a laboratory handling the specimens of Marburg hemorrhagic fever.[9]

Conclusion

Marburg hemorrhagic fever is an uncommon infectious disease. However, its outbreak is a disaster for the affected people and involved area. Better awareness and prevention can keep the disease from spreading. Improved diagnostic tools, more detailed pathophysiology, the specific treatment and even a vaccine are other urgent issues.

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