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Review Article

Marburg virus disease: a brief updated overview

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ABSTRACT

The Marburg virus disease made headlines when Tanzania declared an outbreak on the 23rd of March 2023. Five deaths and three further cases were identified at the time of the announcement. Symptoms of Marburg virus can include fever, headache, muscle aches, vomiting, diarrhoea, and bleeding from various parts of the body, hence the similarity to Ebola which also causes a haemorrhagic fever. There is no specific treatment for Marburg virus, but supportive care can help manage symptoms and improve outcomes. This article aims to update physicians working in primary care on the presentation of Marburg virus disease as well as the latest updates in guidelines implemented to help with its management and prevention.

Keywords: Africa, Tanzania, Marburg, Haemorrhagic fever, Tropical medicine

INTRODUCTION

The Marburg virus disease (MVD) made headlines when Tanzania declared an outbreak on the 23rd of March 2023. Five deaths and three further cases were identified at the time of the announcement. Several outbreaks have been reported since it was first discovered, with the worst being back in 2004 in Angola where the virus was responsible for the 252 cases as well as 227 deaths. Its name derives from the town of Marburg where it was first identified in 1967, when an outbreak occurred in Germany and Yugoslavia among laboratory workers following exposure to the infected monkeys from the Uganda.[1]

The virus is part of the order *Mononegavirales*, the family *Filoviridae*, and the genus *Marburgvirus*. It is primarily found in African countries, most commonly in Uganda and the Democratic Republic of Congo (DRC), and is spread through contact with infected animals or people.[1,2,5,7]

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General practitioners in the UK are expected to

Diagnose and manage diseases of infectious origin commonly seen in returning traveller, promptly and appropriately refer any rare serious infectious diseases, know how to access specialist input when needed, know where to find appropriate travel health information such as treatments and immunisations and recognise and manage medical emergencies in patients with acute or chronic infectious diseases.[15]

EPIDEMIOLOGY AND TRANSMISSION

Marburg virus is primarily found in Africa, particularly in Uganda and the Democratic Republic of Congo (DRC), but cases have also been reported in other countries during a number of outbreaks over the years.

An estimate by researchers in 2022 places 105 million people in areas suitable for the zoonotic transmission for this virus.[3-5]

Marburg virus is believed to be transmitted by a number of ways

Human to human transmission via contact with blood, secretions, bodily fluids, and tissues of infected patients/ deceased. This can easily occur when caring for patients for example and it accounts for most transmissions. Animal-to-human transmission through contact with infected animals, particularly fruit bats also known as *Roussettus aegypticus* or their excrement.

Marburg virus can also be transmitted sexually through semen.[5] Marburg virus outbreaks are rare, but they can be severe and have high mortality rates with high case fatality rates ranging anywhere between 24% and 90% (7). Outbreaks typically occur in remote areas with poor public health infrastructure, making them difficult to contain.[5]

FULL CLINICAL PICTURE

The incubation period for Marburg virus ranges from 2 to 21 days.

Generalisation phase, day 1-5: The patient suddenly encounters flu-like symptoms, high fever, myalgia and fatigue, dysphagia, dyspnea, oedema, and in severe forms can progress to encephalitis, confusion, delirium, irritability, and aggression.

Early organ phase, day 5-13: Patients may develop several hemorrhagic manifestations such as mucosal bleeding, petechiae, hemorrhagic effusions, severe diarrhoea with blood, hematemesis, and leakage from venepuncture sites.

Late organ phase, day 13-20: All of the above can cause severe dehydration and metabolic disturbances. This leads to multiple organ failure, shock and eventually death.[5]

Pathophysiology

Marburg virus targets monocytes and macrophages which results in cellular activation and damage to secondary targets such as endothelial cells. Development of cytokines and other proinflammatory mediators eventually lead to shock which is the primary cause of death in MVD.[13]

Table 1: Differential diagnosis.

Malaria infection	Ebola virus infection
COVID-19	Lassa fever
Typhoid fever	Shigella infection
Dengue fever	Crimean-Congo HF
Influenza infection	Gastroenteritis
Sepsis	Measles

Table 2: Investigations.

Test	Result	Comments
RT-PCR	Positive	Negative doesn't rule out, until 72 hours after onset of symptoms
U+Es	Maybe AKI (high creatinine or urea), maybe hypokalaemia	AKI later on could be indicative of acute tubular necrosis.
FBC	Decreased platelets, decreased leukocytes, neutrophil leukocytosis, low Hb due to bleeding	Initially thrombocytopenia and leucopenia, maybe leukocytosis in later stages, severe cases may lead to DIC
Clotting	Prolonged prothrombin time (PT) or activated partial thromboplastin time (aPTT)	Severe infection may lead to DIC
LFT	Elevated ALT and AST, bilirubin, GGT, ALP typically normal or mildly elevated	AST rise higher than ALT indicative of widespread tissue damage and linked to fatal infection. Extremely high ALT and jaundice may suggest viral hepatitis.
Calcium	Hypocalcaemia	Has been linked to fatal infections
Lactate	Elevated	Indicative or tissue hypoperfusion and shock
Amylase	Elevated in pancreatitis	Pancreatitis may occur in severe cases
Blood cultures	To exclude bacterial sepsis	
ELISA	Filovirus-specific IgM or IgG antibodies	IgM maybe positive days 4-7 and disappear within 1-2 months after recovery, IgG usually develops day 6-18 as well as can persist for the years
Malaria	Maybe positive or co-existing infection	Positive results does not exclude Marburg virus infection

TREATMENT AND MANAGEMENT

There is currently no specific treatment for Marburg virus, but supportive care can help manage symptoms and improve outcomes. This may include fluids and electrolyte replacement, pain management, and treatment of secondary infections. Experimental treatments, such as antiviral drugs and monoclonal antibodies, have shown some promise in animal studies and clinical trials, but more research is needed.[10,11]

The UK health security agency has guidance for managing hemorrhagic fevers including Marburg. It starts by asking the following questions: Does the patient have a fever (≥37.5) OR history of fever in the past 24 hours? Has the patient developed symptoms within 21 days of leaving a viral hemorrhagic fever (VHF) endemic country? Has the patient cared for, come into contact with body fluids, handled clinical specimens (blood, urine, faeces or cultures) from an individual or laboratory animal known or strongly suspected to have VHF within the past 21 days?

The above questions would lead to one of two outcomes

Low possibility of VHF

Urgent malaria investigation and urgent local investigations as normally appropriate and including blood cultures.

High possibility of VHF

Patient isolated in a side room, urgent malaria investigation, full blood count, U and Es, LFTs, clotting screen, CRP, glucose and blood cultures and inform laboratory of possible VHF case (for specimen waste disposal purposes if confirmed).

If the diagnosis is likely then the case should be discussed with the infectious diseases consultant who in turn will discuss the VHF test with the imported fever service. Once the diagnosis is confirmed, the patient is transferred to a high level isolation unit.[6,7]

PREVENTION AND CONTROL

Prevention of Marburg virus infection involves avoiding contact with infected animals and practising good hygiene, such as frequent hand washing and avoiding contact with bodily fluids from infected individuals. Control measures during outbreaks typically involve isolation and quarantine measures, contact tracing, and public health education campaigns. There is currently no licensed vaccine for Marburg virus, but several candidates are in development.[6,7]

The Centers for Disease Control (CDC) has guidelines and training material known as The infection prevention and control (IPC) for MVD. It aims to train frontline healthcare staff on methods to reduce transmission. The training sessions can range from 15-25 minutes and the documents are available on the CDC website.

Travellers to affected areas mentioned above should avoid contact with people presenting with fever, myalgia, diarrhoea, weakness or bleeding. They should also be on the lookout for symptoms till 21 days.

FUTURE EFFORTS

Ongoing research efforts are focused on developing new treatments and preventative measures for Marburg virus.

This first-in-human trial of cAd3 (Chimpanzee adenovirus type 3-vectored vaccine) showed the agent is safe and immunogenic, with a safety profile similar to cAd3-vectored filovirus vaccines. It was given to 40 healthy adult participants, none of whom experienced serious adverse events[8,9]

There is also the development of vaccines such as the rVSVΔG-ZEBOV-GP vaccine, which has shown efficacy against both Ebola and Marburg viruses in preclinical studies. Other approaches include the development of monoclonal antibodies, RNA-based therapeutics and gene editing techniques.[13,14]

CONCLUSION

Marburg virus disease is a condition which travellers to the region must be aware of. The condition can progress and reach a fatal stage if left untreated, which is something clinicians need to be familiar with to provide travellers with the necessary precautions. In the event a person is affected then they will need to follow the latest guidance which is supported by the CDC.

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