53

A 24-Year-Old Woman from Uganda With Fever and Shock

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Clinical Presentation

History

A 24-year-old woman presents to a small hospital in rural Uganda because of a 5-day history of a febrile illness. Apart from fever, the illness started with a sore throat and aching all over. She also developed some abdominal pain and diarrhoea. The patient has become increasingly unwell over the course of the past days. She is very weak and needs help to stand.

Her husband died of a severe febrile illness 6 days before she became ill. He had worked in a local gold mine and had previously been in good health. He had fallen ill about a week before his death. His wife had looked after him during his final illness and he had died at home.

Clinical Findings

The patient looks very unwell. Her blood pressure is 85/65 mmHg, pulse rate 105 bpm, temperature 38°C (100.4°F). She has bilateral conjunctivitis. There is no rash and no lymphadenopathy. The heart sounds are normal and her chest is clear. Her abdominal examination is normal.

Questions

1. What are your differential diagnoses?
2. How would you approach the patient and what tests would you do?

Discussion

A young Ugandan woman presents to a rural hospital with a severe febrile illness. She is hypotensive and has bilateral conjunctivitis. Her husband has recently died after a short febrile illness.

Answer to Question 1

What Are Your Differential Diagnoses?

The presentation is non-specific and a wide range of acute infectious diseases are possible.

Both malaria and typhoid fever present with non-specific symptoms and a septic picture, but neither would cause conjunctivitis. Other causes of bacterial sepsis, including invasive meningococcal disease have to be considered.

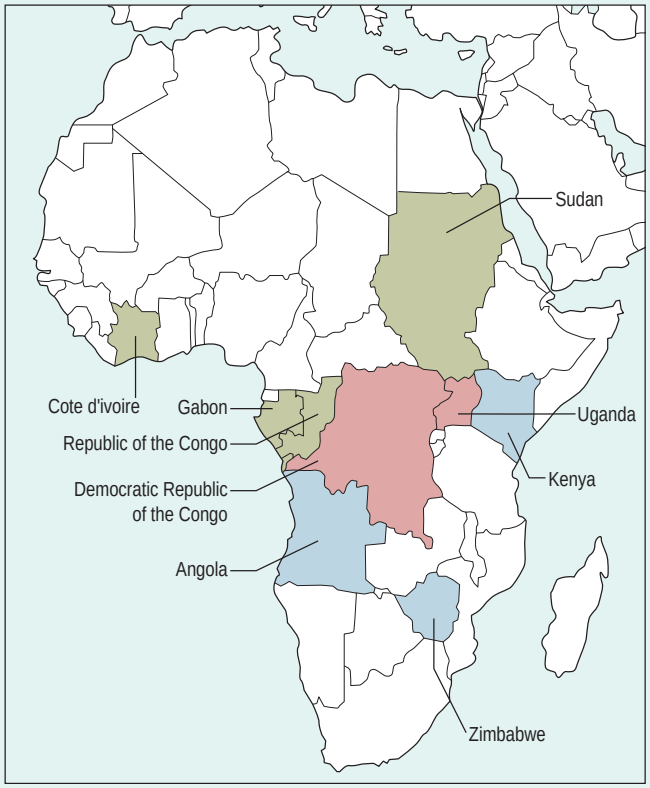
A severe viral infection with an adenovirus or influenza would be possible but the patient appears slightly too unwell for this. Measles commonly presents with pronounced conjunctivitis, but at this stage one would see a rash. Zika virus was discovered in Uganda and presents with conjunctivitis, but usually is a mild viral illness and does not cause shock.

The fact that the patient's husband has recently died of a similar severe febrile illness should raise the suspicion of a viral haemorrhagic fever (VHF). Marburg virus disease (MVD) has been associated with mines.

Answer to Question 2

How Would You Approach the Patient and What Tests Would You Do?

The patient should be treated with extreme caution because of the possibility of a viral haemorrhagic fever. Nosocomial spread of these diseases can cause hospital outbreaks with a high case fatality rate. The patient should ideally be isolated in a side room. Blood tests should be kept to a minimum to reduce the risk to laboratory staff. Protective clothing, such as gloves and a surgical gown, are recommended during procedures. The risk of transmission of VHF viruses from a malaria slide is very low once the blood spot is dry; therefore it would be reasonable to do a malaria slide or a rapid diagnostic test. However, the prevalence of *Plasmodium falciparum* parasitaemia in Uganda is high and a positive slide would not rule out VHF.



• **Fig. 53.1** Endemic areas for filoviruses. Only filoviruses known to cause haemorrhagic fever are shown. Countries where Ebola and Marburg haemorrhagic fevers have been seen are indicated in green and blue, respectively, with countries in red indicating documentation of both diseases. Incidence and risk of disease may vary significantly within each country. Filoviruses are likely to occur outside these countries but have not yet been recognised. (Reproduced from Farrar, J., Hotez, P., Junghanss, T., et al., 2013. Manson's Tropical Diseases. Farrar, J., Ed. London: Elsevier. Fig. 16.1.)

To protect laboratory staff all biochemical and haematological tests should be done using near-patient testing if possible.

The public health authorities should be alerted to the possibility of a case of viral haemorrhagic fever. Ideally testing for this should be organized, but samples are likely to need special shipping arrangements to be taken to a specialized laboratory.

The Case Continued…

A presumed diagnosis of Marburg virus disease was made. The malaria slide showed a low level of parasitaemia with *P. falciparum.* A sample for Marburg and Ebola PCR was sent in a sealed plastic container. The patient was isolated in a side room and all patient contact was carried out while wearing gloves. She was treated with IV artesunate and then artemether/lumefantrine. She was given empirical IV ceftriaxone to cover for possible sepsis and was resuscitated with IV fluids.

Over the next few days the patient remained very unwell, then she started to improve. Once she had recovered, she was kept in isolation for an additional 2 days and was then allowed to return home. The day after her discharge a positive Marburg virus PCR result came back. Had this been known while she was in the hospital, stricter infection control procedures, including double gloves, a mask, goggles and a disposable (waterproof) surgical gown, would have been appropriate.

Her family members, close friends and medical staff were interviewed; anyone who had had physical contact with her, or her body fluids, was told to monitor their temperature for 21 days from the time of contact which is the maximum incubation period for MHF. Anyone who developed a fever or became unwell during this period was isolated.

SUMMARY BOX

Filoviral Diseases

Marburg virus disease (MVD) and Ebola virus disease (EVD) are both caused by filoviruses. They are clinically virtually indistinguishable and cause severe illnesses with a high case fatality rate. Symptoms are non-specific, and patients may present with fever, sore throat, general body ache, retrosternal chest pain and abdominal symptoms. Conjunctivitis is common. The most frequent cause of death is shock. Less than half of those who die develop haemorrhages because of disseminated intravascular coagulation.

Because symptoms are non-specific and testing is difficult in most of Africa, filoviral haemorrhagic fevers (FHF) are normally recognized only if a cluster of cases occurs. In particular, an outbreak in an endemic area in which health workers die should raise the suspicion towards FHF.

EVD and MVD have both been detected over wide areas of sub-Saharan Africa. Both are zoonoses of bats. Many cases of MHF have been linked to entering or working in caves or mines, whereas cases of EHF are associated with butchering and eating apes or monkeys.

Filoviruses can spread between people through direct physical contact or contact with infected body fluids. Large nosocomial outbreaks involving the death of large numbers of medical staff have been recorded. Therefore strict infection control measures should be followed while caring for anyone with a suspected viral haemorrhagic fever. Vaccines against MVD are under development but have not yet been tested on humans.

The preferred method of testing for MVD is with PCR, antigen detection tests are less sensitive and specific. The treatment of MVD is supportive. Treatments which have shown promise in EVD, such as antibody therapies e.g. ZMAPP or the antiviral drug favipiravir, have not been clinically tested in humans with MVD.

Further Reading

1. Blumberg L, Enria D, Bausch DG. Viral Haemorrhagic Fevers. In: Farrar J, editor. Manson's Tropical Diseases. 23rd ed. London: Elsevier; 2013 [chapter 16].
2. Emanuel J, Marzi A, Feldmann H. Filoviruses: Ecology, Molecular Biology, and Evolution. Adv Virus Res 2018;100:189–221 [chapter 9].
3. Bauer MP, Timen A, Vossen ACTM, et al. Marburg haemorrhagic fever in returning travellers: an overview aimed at clinicians. Clin Microbiol Infect 2019;21:e28–e31.
4. World Health Organization. Clinical management of patients with viral haemorrhagic fever, a pocket guide for front-line health workers, ISBN 978 92 4 154960 8 (NLM classification: WC 534). http://apps.who.int/medicinedocs/documents/s22501en/s22501en.pdf.