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Brief Report

Autopsy Findings of a Co-Incidental Postmortem Done on a Confirmed Marburg Virus Patient in Uganda

Samuel Kalungi [1], Henry Kyobe Bosa [2,3,4,*], Misaki Wayengera [5] and Michael Odida [6]

[1] Senior Consultant Pathologist, Mulago Supra-National Reference Hospital, Kampala, Uganda,
[2] Incident Commander, Incident Management Team, Ministry of Health, Kampala, Uganda
[3] Consultant Epidemiologist, Uganda Peoples Defense Forces, Kampala, Uganda
[4] Senior Research Scientist, Vaccine and Epidemics Research Group, Makerere Lung Institute, Kampala, Uganda
[5] Chair- Uganda MoH Ministerial Scientific Advisory Committee on Epidemics & Dangerous Pathogens/Makerere University, Kampala, Uganda
[6] Professor, Pathology Department, Gulu University, Gulu, Uganda
* Correspondence: hskyobe@gmail.com

Abstract

Background: Marburg virus disease (MVD) is a viral hemorrhagic fever caused by species members of the *Marburgvirus* genera, family *Filoviridae*. Clinical manifestations resemble those of the other generic Viral Hemorrhagic Fevers—like ebola virus disease (EVD). Because of biosafety and bio-risk concerns arising from the highly infectious nature of filoviruses, postmortems are generally contra-indicated. Thus, description of gross pathological and histopathological findings remains poor. Here, we describe the autopsy findings following a rare co-incidental post-mortem done on a 30 male patient, later confirmed to have MVD. **Results**: (a) External examination revealed body of a male adult in good nutritional state and no external injuries; (b) Internal examination showed mild ascites in the peritoneal cavity with marked pallor of internal organs. The stomach and intestines were filled with blood without any focal organic lesions. There were petechial hemorrhages in the sub-pleura of both lungs, but no focal lesions in lungs. The other organs had no gross lesions; (c) Microscopic examination of lung, kidney and liver detailed marked intra-alveolar hemorrhages, tubular necrosis in the kidneys and extensive necrosis in the liver with foci of thrombi in major vessels; (d) a diagnosis of massive hemorrhage and disseminated intravascular coagulation (DIC) was made; and immediate cause of death attributed to hemorrhagic shock. **Conclusions**: MVD is associated with intra-luminal GIT hemorrhage and DIC in major organs (lungs, kidneys, & liver) resulting in focal or extensive necrosis. Malaria co-infection, in absence of early specific biomarkers may have delayed the suspicion for a VHF in this patient. To enhance early detection of VHFs, there is a need for early biomarkers of VHFs.

Keywords: Marburg virus disease; disease outbreak ; autopsy

1. Introduction

On 27th September 2024, the Ministry of Health of Rwanda declared a still on-going outbreak of Marburg Virus disease (MVD) characterized by clusters of infection and transmission among health care workers (HCWs). As of 10th October, 58 confirmed cases (29 HCWs) and 13 deaths had been recorded with 5 recoveries.

Ebolavirus and *Marburgvirus* are two genera of negative–stranded RNA viruses belonging to the family *Filoviridae* [1,2]. Filoviruses have historically been the cause of rare but fatal viral hemorrhagic fevers (VHF) within remote villages of equatorial Africa [3–5]. A member of the genus *Marburgvirus*

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was first isolated in 1967 during outbreaks in Germany and Yugoslavia. These outbreaks were linked to infected monkeys imported from Uganda [2]. Members of the genus *Ebolavirus*, on the other hand, first emerged in 1976 as the causative agent of two simultaneous VHF outbreaks in southern Sudan and northern Zaire [1,3]. Since then, species (*spp*) of the two genera have caused several outbreaks of VHFs, some designated public health emergencies of international concern (PHEIC) [3,4].

The first recognized outbreak of Marburg virus disease (MVD) on the Africa continent occurred in February 1975 in Rhodesia and involved a young Australian tourist who died on the seventh day from hemorrhage resulting from a combination of disseminated intravascular coagulation and hepatic failure, as the index case. Two secondary cases accrued but survived. In 1980, two cases of MVD occurred in Western Kenya: the patient's attending physician in Nairobi being the second case. In 1987, another fatal case of MVD happened in a young man who had traveled extensively in Kenya [5]. Ten years later, an outbreak of MVD occurred in 1998 in northeastern Democratic Republic of Congo, representing the second largest outbreak on the continent. The epicenter of the outbreak was the village of Durba in the Haut-Uélé District, Oriental Province. Because of the remoteness of the area and the fact that a civil war was occurring, access to the area and evaluation of the disease were delayed until May 1999, when an international team of investigators was able to perform studies. These investigators identified 73 cases (8 laboratory-confirmed and 65 suspected). Subsequent follow-up surveillance identified more than 150 cases through December 2000. Finally, in April 2005, the largest ever recorded outbreak of MVD occurred in Uige province, Angola. By June, the Ministry of Health in Angola had reported a total of 422 cases and 356 deaths in Uige Province [5]. More recently, Equatorial Guinea has had recurrent outbreaks of MVD in the last 3 years, and Tanzania recorded an outbreak of MVD in 2023.

Of particular concern today, is that the incidence of MVD has increased in sub-Saharan Africa, possibly due to increased human activities that raise the chance of contact between humans and filovirus host animals or birds within the wild. Uganda alone has experienced 4 outbreaks of MVD in the past 20 years, resulting in fatalities and socioeconomic effects from loss of tourism. The first recorded outbreak of MVD in Uganda occurred in the Kamwenge district in 2007, where 4 MVD cases were confirmed in miners at the Kitaka mine. A second, larger outbreak occurred in the western Uganda districts of Kabale, Ibanda, and Kamwenge in 2012.; being linked to mining activity in the Ibanda district. In addition, isolated outbreaks have been recorded in tourists from the United States and the Netherlands infected in western Uganda when they visited Python Cave in Queen Elizabeth National Park in 2008. Whereas the clinical manifestations of MVD are known to closely mimic those seen in ebola virus disease (EVD); the pathological findings in MVD have not been well documented as for EVD (whose postmortem findings have mostly inferred from autopsies of infected non-human primates, due to the contra-indication against postmortems in both EVD and MVD) [6–10]. There have been recent attempts to elucidate the pathology of MVD within guinea pigs and rhesus macaques [11–13]. In 2014, an isolated fatal case of MVD occurred in Uganda [14].

This paper describes the autopsy findings following a rare co-incidental post-mortem done on the patient who was later confirmed to have MVD.

2. Materials and Methods

3. Results

3.1. The case under scrutiny has already been previously documented by Nyakaharuka L, *et al* (2017) [14]. Briefly, on September 23, 2014, a healthcare worker was hospitalized at Mengo Hospital on the outskirts of Kampala in Uganda. He was hospitalized with an acute febrile illness with features consistent with a viral hemorrhagic fever (VHF). The individual was a 30-year-old male, a radiographer at Mengo Hospital. He was reported ill 6 days prior to hospitalization where he was tested positive for malaria by rapid diagnostic test. Overt hemorrhagic signs that included profuse nasal bleeding began 6 days from onset of symptoms; other findings included a high-grade fever with average temperature 38.4°C. By the time of death,11 days from onset of symptoms, he had several

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nonspecific symptoms that included nausea, vomiting, diarrhea, musculoskeletal pain, abdominal pain, headache, sore throat, difficulty swallowing, difficulty breathing, anorexia, bloody stools, and features of what appeared to be upper upper gastrointestinal tract bleeding. Gross anatomy postmortem was done on 28th September 2014 where whole blood and serum samples were collected and analyzed at Uganda Virus Research Institute (UVRI)/US Centers for Disease Control and Prevention (CDC) VHF laboratory in Entebbe for testing real-time reverse transcription PCR (RT-PCR) targeting the MARV NP gene antigen detection, and MARV IgM ELISA were detected on the as described by Nyakarahuka L et al [14]. Although MARV by RT-PCR, antigen detection and IgM serologic results were negative on ELIZA. Tie-breaker confirmation was obtained from duplicate whole blood and serum samples by using RT-PCR primers and probes targeting MARV VP40 gene and a commercial filovirus PCR screening assay (Altona Diagnostics, Hamburg, Germany). Specifically, based on the two positive RT-PCR, MVD was confirmed in this patient. Samples were also shipped specimens to the CDC Viral Special Pathogens Branch, Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases (Atlanta, GA, USA), for further testing, including virus isolation and sequencing. Here, a virus isolate (812601) was generated from the clinical specimen after a single passage in cell culture (Vero E6).

3.2. Circumstances of Death & Autopsy Request

On 29th September 2014, the senior author of this paper, then a senior consultant pathologist in the hospital carried out an autopsy on a 30-year-old male radiographer, who had been suspected of a VHF. At In absence of a timely positive laboratory diagnosis of MVD, the attending physicians had sustained a differential diagnosis of upper gastro-intestinal bleeding as the cause of death. Under these circumstances, a postmortem was requested against the set contra-indications for doing so in cases of filovirus VHFs. It is curious that no suspicion was raised at the time by both clinical and pathology teams. Nevertheless, samples taken off a day prior to the patient's demise for further laboratory investigation and testing at the Uganda Virus Research Institute (UVRI) in Entebbe, returned after 3 days pointing to positive diagnosis of MVD. The Pathologist and mortuary attendants present during the autopsy, as well as the attending physicians and nurses on ward were subsequently notified of the findings; and told to undergo mandatory self-isolation at home for 21 days. No secondary cases occurred among all 17 health workers closely linked to the care of this patient. *The low infectivity MVD in this case is poorly understood in comparison to a cluster of healthcare workers who were similarity exposed to sudan ebolavirus (SUDV) species during the 2022-2023 outbreak in Uganda, where a cluster of 6 health workers (the surgeon, anesthetist, intern, and 2 residents) exposed during a co-incidental surgery done to halt a suspected upper GIT bleed, all got infected and 1 died .*

3.3. Postmortem Findings in MVD

External examination revealed the body of a male adult in good nutritional state and no external injuries, ruling out any traumatic causes. These findings are consistent with the fact that no peripheral stigmata to suggest VHF may be found following external examination of the body of a filovirus VHF victim. This can put unsuspecting pathologists at increased risk for undertaking autopsies if no clinical symptomatology is present to them, as was seen in this case.

3.4. Internal examination showed mild ascites in the abdominal cavity with marked pallor of internal organs. The stomach and intestines were filled with blood without any focal organic lesions. There were petechial hemorrhages subpleura of both lungs, but no focal lesions in lungs. The other organs had no visible gross lesions. Generally, previous gross autopsy findings for EVD have been documented to include petechiae or ecchymoses of the skin or mucous membranes, and hemorrhage of internal organs. However, these pathological features are seen in many other diseases and raise a broad differential diagnosis, which includes not only other VHFs but also rickettsial, bacterial, other viral and even non-infectious causes of hemorrhage [6–10].

4. Discussion

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Overall, several cellular receptors (such as asialoglycoprotein, Lectin C DC-SIGN and DC-SIGNR; as well Neimann P C1) seem to explain the differential tissue and organ tropism of both ebolavirus and Marburgvirus, in the host [15–18]. Here, microscopic examination of lung, liver and kidneys detailed marked intra-alveolar hemorrhages, extensive necrosis in the liver with foci of thrombi in major vessels, and tubular necrosis in the kidneys. Elsewhere, Microscopic examination of lung, liver and kidneys for fatal EVD cases have revealed closely similar findings as those reported for this case [18]. Specifically, the lungs from fatal EVD cases show congestion, focal intra-alveolar oedema and hemorrhage with no significant inflammation. Immunohistochemistry (IHC) shows viral antigens in alveolar macrophages, endothelial cells, fibroblasts and other interstitial cells [18–22]. The liver, on their hand, has been shown to have the most characteristic histopathological features in filovirus infections. Hepatocyte necrosis ranges from focal to widespread, often with minimal inflammation. Mild to moderate small-droplet steatosis and Kupffer cell hyperplasia are also seen. In EBOV, the portal tracts usually exhibit extensive karyorrhexis and mononuclear inflammatory cell infiltrates. Hepatocytes may show characteristic intracellular eosinophilic and filamentous or oval virus inclusions, which are predominantly found in periportal zones and surrounding areas of necrosis [23–25]. Lastly, kidneys frequently show evidence of acute tubular necrosis with no significant inflammation. IHC shows endothelial (including glomerular capillary loops), focal interstitial and tubular staining. Apoptotic debris is frequently seen in the areas of interstitial staining [11,12,17].

A diagnosis of massive hemorrhage and disseminated intravascular coagulation (DIC) was made; and immediate cause of death attributed to hemorrhagic shock. This was an accurate and consistent diagnosis despite the absence of laboratory results to confirm MVD. Taken together, the above findings suggest that MVD, like EVD, is associated with intra-luminal GIT hemorrhage and DIC in major organs (lungs, kidneys, & liver) resulting in focal or extensive necrosis.

5. Conclusions

In conclusion, we report the autopsy findings following a rare co-incidental post-mortem done on the patient who was later confirmed to have MVD. The salient findings suggest that MVD is associated with intra-luminal GIT hemorrhage and DIC in major organs (lungs, kidneys, & liver) resulting in focal or extensive necrosis.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

Author Contributions: "Conceptualization, M.W, H.K.B. and S.K.; methodology, M.O, S.K,M.W; writing—original draft preparation, , M.W.; writing—review and editing, M.W, H.K.B, S.K and M.O. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

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MDPI	Multidisciplinary Digital Publishing Institute
DOAJ	Directory of open access journals
TLA	Three letter acronym
LD	Linear dichroism

References

1. Feldmann H, Slenczka W, Klenk HD. Emerging and reemerging of filoviruses. *Arch Virol Suppl.* 1996;11:77–100.
2. Siegert R, Shu HL, Slenczka HL, *et al*. The aetiology of an unknown human infection transmitted by monkeys (preliminary communication). Ger Med Mon. 1968;13:1–2.
3. Towner JS, Sealy TK, Khristova ML, et al. Newly discovered Ebola virus associated with hemorrhagic fever outbreak in Uganda. *PLoS Pathog*. 2008;4(11):e1000212.
4. Bausch DG, Nichol ST, Muyembe-Tamfum JJ, *et al*. Marburg hemorrhagic fever associated with multiple genetic lineages of virus. *N Engl J Med.* 2006;355(9):909–919
5. Ligon BL. Outbreak of Marburg hemorrhagic fever in Angola: a review of the history of the disease and its biological aspects. Semin Pediatr Infect Dis. 2005; 16(3):219-224.
6. Osborn M, Lucas S, Burton J. Autopsy in patients with confirmed or suspected Ebola virus disease (Ebola haemorrhagic fever). RCPath. 2014 (Sept). Available at URL: https://www.rcpath.org/static/4d909335-62e9-47b9-b1adaf170bc9df0a/pubs_ebolaautopsy_sept14_v2.pdf
7. Gedigk P, Korb G, Bechtelsheimer H. The pathological anatomy of the Marburg virus disease. *Verh Dtsch Ges Pathol* 1968; 52: 317–320.
8. Rippey JJ, Schepers NJ, Gear JH. The pathology of Marburg virus disease. *S Afr Med J* 1984; 66: 50–54.
9. Baskerville A, Bowen ET, Platt GS, et al. The pathology of experimental Ebola virus infection in monkeys. *J Pathol* 1978; 125: 131–138.
10. Geisbert TW, Young HA, Jahrling PB, *et al.*Pathogenesis of Ebola hemorrhagic fever in primate models: evidence that hemorrhage is not a direct effect of virus-induced cytolysis of endothelial cells. *Am J Pathol* 2003; 163: 2371–2382.
11. Cooper TK, Sword J, Johnson JC, et *al*. New Insights Into Marburg Virus Disease Pathogenesis in the Rhesus Macaque Model. *J Infect Dis*. 2018 ;218(suppl_5):S423-S433.
12. Cooper TK, Huzella L, Johnson JC, et al. Histology, immunohistochemistry, and in situ hybridization reveal overlooked Ebola virus target tissues in the Ebola virus disease guinea pig model. *Sci Rep.* 2018; 8(1):1250.
13. Becker S, Spiess M, Klenk HD. The asialoglycoprotein receptor is a potential liver-specific receptor for Marburg virus. *J Gen Virol* 1995; 76: 393–399.
14. Nyakarahuka L, Ojwang J, Tumusiime A, et al. Isolated Case of Marburg Virus Disease, Kampala, Uganda, 2014. *Emerg Infect Dis*. 2017 ;23(6):1001-1004.
15. Alvarez CP, Lasala F, Carrillo J, et al. C-type lectins DC-SIGN and L-SIGN mediate cellular entry by Ebola virus in *cis* and in *trans*. *J Virol* 2002; 76: 6841–6844.
16. Simmons G, Reeves JD, Grogan CC, et al. DC-SIGN and DC-SIGNR bind Ebola glycoproteins and enhance infection of macrophages and endothelial cells. *Virology* 2003; 305: 115–123.
17. Carette JE, Raaben M, Wong AC, et al. Ebola virus entry requires the cholesterol transporter Niemann–Pick C1. *Nature* 2011; 477: 340–343.
18. Martines RB, Ng DL, Greer PW, Rollin PE, Zaki SR. Tissue and cellular tropism, pathology and pathogenesis of Ebola and Marburg viruses. J Pathol. 2015;235(2):153-174.
19. Twenhafe NA, Mattix ME, Johnson JC, *et al.*Pathology of experimental aerosol Zaire Ebola virus infection in rhesus macaques. *Vet Pathol* 2013; 50: 514–529.
20. Lalle E, Biava M, Nicastri E, et al. Pulmonary Involvement during the Ebola Virus Disease. *Viruses*. 2019;11(9):780.
21. Smither SJ, Nelson M, Eastaugh L, *et al.*Experimental respiratory Marburg virus haemorrhagic fever infection in the common marmoset (*Callithrix jacchus*). *Int J Exp Pathol* 2013; 94: 156–168.
22. Zaki SR, Paddock CD. Viral diseases. In *Pulmonary Pathology*, 1st edn, DS Zander, CF Farver (eds). Churchill Livingstone Elsevier: Philadelphia, 2008; 245–286.

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23. Ellis DS, Simpson IH, Francis DP, *et al.*Ultrastructure of Ebola virus particles in human liver. *J Clin Pathol* 1978; 31: 201–208.
24. Bechtelsheimer H, Korb G, Gedigk P. The morphology and pathogenesis of 'Marburg virus' hepatitis. *Human Pathol* 1972; 3: 255–264.
25. Bechtelsheimer H, Korb G, Gedigk P. The 'Marburg-virus'-hepatitis. Studies in man and guinea pigs. *Virchows Arch A Pathol Pathol Anat* 1970; 351: 273–290.

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