Case Study

Unraveling the Pathology of the Rare Marburg Virus Disease Through Autopsy: A Case Report

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Abstract

Marburg virus disease is a rare, highly infectious, and fatal illness with limited autopsy-based studies. This case report details the autopsy findings of a woman who died of Marburg virus disease, offering valuable insights into the pathogenesis of the disease and its effects on various organ systems. The patient initially presented with fever, nausea, joint pain, and fatigue, which rapidly progressed to multiorgan failure and disseminated intravascular coagulopathy. Autopsy revealed extensive hemorrhagic manifestations, including ecchymoses, purpura, and petechiae, on both external and internal surfaces. Significant hemorrhagic effusions were observed in the body cavities, and multiple organs showed signs of congestion, hemorrhage, and edema.This case report contributes to the limited autopsy-based literature on Marburg virus disease, emphasizing the importance of considering it in the differential diagnosis of febrile illnesses in endemic areas and the need for further comprehensive autopsy studies to guide targeted interventions.

Keywords: Marburg virus disease; Autopsy findings; Hemorrhagic fever; Multiorgan failure; Febrile illness; Disseminated intravascular coagulation

Background

Marburg virus disease (MVD), formerly known as Marburg hemorrhagic fever, is a severe, highly contagious, and fatal illness caused by Marburg and Ravn viruses[1]. It was initially detected in 1967 after two simultaneous outbreaks in Germany and Serbia, which were associated with laboratory work using African green monkeys imported from Uganda[2]. Human MVD infection initially results from exposure to Rousettus fruit bats, and then spreads through direct contact with the bodily fluids of infected individuals[3]. Outbreaks and sporadic cases of this rare but highly infectious disease have been reported in Africa [4]. MVD presents significant challenges for healthcare systems owing to its rapid progression, rarity, high mortality rate, and potential

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transmission[5]. Autopsy plays a crucial role in understanding the pathophysiology of MVD and its effects on different organ systems [6]. However, owing to its rarity and high rate of infectivity and mortality, autopsy is infrequently performed for MVD deaths [7]. This limitation has resulted in gaps in our knowledge regarding the correlation between clinical manifestations, disease progression, and its effects on various organ systems[8].

This case report discusses the autopsy of a 35 years old female patient who died of MVD, offering valuable insights into the pathogenesis of the disease and its effects on various organs. By analyzing the macroscopic changes observed during the post-mortem examination, we aim to enhance the current understanding of the relationship between clinical symptoms and specific organ involvement in MVD and potentially guide future diagnostic and treatment strategies. Additionally, this study addresses gaps in the literature concerning the relationship between clinical symptoms and autopsy findings in patients with Marburg Virus Disease.

Case Presentation

History

The Ministry of Health officially announced a nationwide state of emergency on September 27, 2024, due to the MVD outbreak, which was subsequently declared its end on December 20, 2024. On September 18, 2024, a 35-year-old female patient visited a hospital with a five-day history of fever, nausea, joint pain, and generalized fatigue, with a body temperature of 37.6 °C. She was then diagnosed with an unspecified infection and treated with Augmentin and paracetamol on an outpatient basis. The following day, she returned to the hospital with worsening of the initial symptoms, and her body temperature was 39 °C with signs of dehydration. She was admitted to the inpatient clinic with a clinical diagnosis of acute malaria and treated with IV artesunate, ceftriaxone, and paracetamol. On September 20, 2024, acalculous cholecystitis was confirmed and intravenous metronidazole treatment was initiated. The patient's liver function and complete blood count were investigated, and the results indicated a slight increase in liver enzyme levels with thrombocytopenia. Malaria-thick smears were performed, which yielded negative results. Chest radiography showed only blunt costo-diaphragmatic angles, and chest CT tomography revealed mild bilateral pleural effusion. Abdominal ultrasonography and CT tomography indicated mild ascites and acalculous acute cholecystitis.

Despite these interventions, the patient deteriorated and experienced three episodes of diarrhea. Further investigations showed deteriorating liver and kidney function and an increase in right pleural effusion. For this, a right pleural tap was performed, which resulted in draining 700 ml of fluid. On September 22, 2024, she developed hypoxia, requiring high-flow oxygen therapy, and the treatment for cholecystitis was switched to intravenous meropenem. By September 23, 2024, the patient was confused with worsening hypoxia and developed cardiac arrest. Despite two and a half hours of advanced cardiopulmonary resuscitation, the patient died. The cause of death was classified as disseminated intravascular coagulopathy (DIC) resulting from multiorgan failure due to sepsis originating from gastrointestinal tract infection.

Autopsy findings

Ecchymoses were detected on the right lateral side of the chest wall, epigastric area, inner and back parts of the upper third of the right arm, and injection sites (Figure 1). The conjunctiva of both eyes showed yellowish discoloration and petechial hemorrhage. The oral and nasal orifices were occluded with cotton as part of postmortem care. Rigor mortis was not present on the extremities.

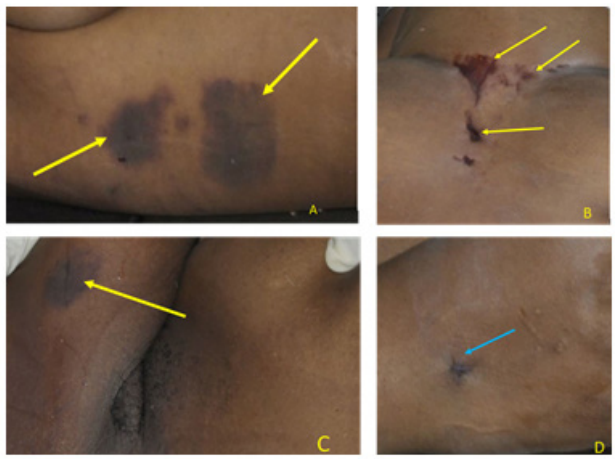

Figure 1:Ecchymoses underneath the skin on the;

A. Right lateral side of the chest wall (Yellow arrows).

B. Epigastric area, the site of cardiopulmonary resuscitation (yellow arrows).

C. Posterior aspect of the proximal third of the right arm (yellow arrow).

D. Sutured injection sites on the dorsum of the right hand (blue arrow).

Internal examination revealed ecchymosis, purpura, and petechia on soft tissues of the anterior neck, pharynx, larynx, esophagus, and trachea (Figure 2). The outer surface of the heart and endocardium displayed petechiae and purpura, respectively (Figure 3). The thoracic cavity contained a significant amount of blood with ecchymoses on the lower third of the inner surface of the left lateral aspect of the chest wall(Figure 4A). The pericardial and pleural cavities were effused, with large amounts of blood-tinged fluid. The lungs were heavier and showed signs of edema, bleeding, and consolidation. The peritoneal cavity was filled with a substantial amount of blood (Figure 4B). The stomach was filled with a large quantity of blood and showed hyperemia of the mucosal lining. The liver appeared pale yellow, with petechial hemorrhages on its surface and multiple internal hemorrhages. The spleen was enlarged, darker red, and friable. The gallbladder exhibited diffuse mucosal hyperemia. The pancreas and kidneys showed signs of congestion and hemorrhage. The brain appeared swollen with a grossly bloody appearance of cerebrospinal fluid. There was no evidence of injury. All the other examination findings were normal.

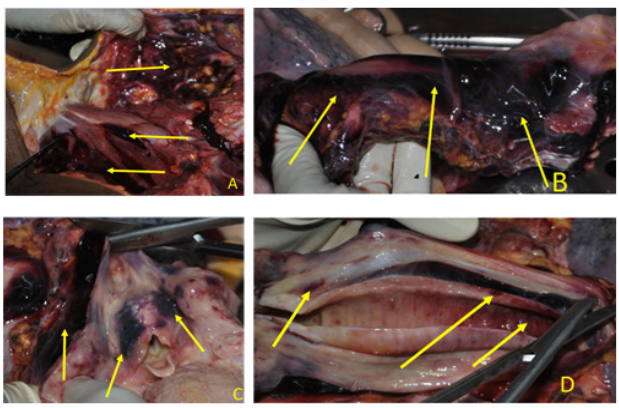

Figure 2: Ecchymosis, purpura, and petechiae on soft tissues and organs of the neck;

A. Reflection of the platysma muscle showing diffuse hemorrhage over the muscle compartments and subcutaneous tissues (yellow arrows).

B. Soft tissues at the posterior aspect of the esophagus and trachea showing diffuse hemorrhage (yellow arrows).

C. The hypopharynx, larynx, and soft tissues of the anterior aspect of the trachea showing hemorrhage (yellow arrows).

D. The inner and outer walls of the esophagus and trachea showing hemorrhage (yellow arrow).

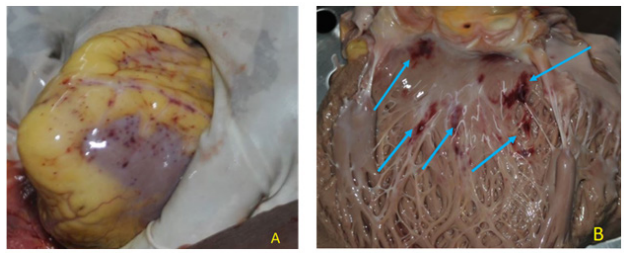

Figure 3: Petechiae and purpura on the heart;

A. The surface of the heart apex showing petechial hemorrhages.

B. Endocardium of the left ventricle showing purpura and petechial hemorrhages (blue arrows).

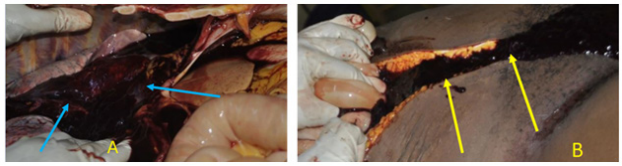

Figure 4: Extensive hemorrhagic effusion in the body cavities;

A. The left side of the thoracic cavity showing extensive effusion with blood after reflection of the left lung (blue arrows).

B. The peritoneal cavity showing a massive amount of blood escaping to the autopsy table through the pelvic area (yellow arrows)

Blood samples were collected to investigate Marburg virus infection, and reverse transcriptase polymerase chain reaction (RT-PCR) confirmed a positive result for Marburg virus disease. Tissue samples from the lungs, liver, brain, kidneys, and heart were collected for histopathological examination and blood, urine, gastric contents, and bile samples were collected for toxicological analysis. However, before

conducting the analysis, these samples were disposed of following biosafety protocols to minimize the risk of virus spread. The final autopsy report concluded that MVD was the underlying cause of death.

Discussion

MVD is a rare and highly infectious disease known for its rapid progression and high fatality rate, resulting in deadly outbreaks; however, its organ-specific pathology remains underexplored.[6,9] Thorough autopsy is crucial for understanding the pathophysiology and specific organ system effects of these diseases [10]. Nevertheless, to the best of our knowledge, studies on autopsy-based MVD are limited. This study details the autopsy of a female patient who succumbed to MVD with signs of acute febrile illness and extensive spontaneous hemorrhage, offering insights into the autopsy findings of a patient with MVD, thereby enhancing our understanding of this rare disease.

MVD is primarily transmitted through direct contact with bodily fluids of an infected person, animal, or contaminated objects. Once the virus penetrates the skin or mucous membranes, it enters the bloodstream or lymphatic system by targeting monocytes, macrophages, and dendritic cells, where it begins to replicate before further spreading to hepatocytes, endothelial cells, fibroblasts, and epithelial cells[3]. Significant viral replication then takes place in the vital organs, such as the spleen, liver, and secondary lymphoid tissues, leading to a cytokine storm and compromising of the humoral immune response[5]. This dramatic immune system dysfunction causes an increase in vascular permeability, tissue damage, and DIC, leading to three phases of disease manifestations: the initial generalization phase, early organ phase, and late organ or convalescence phase[11]. In this case, the patient was initially diagnosed with an unspecified infection, which was subsequently revised to acute malaria and eventually cholecystitis, and appropriate treatment was provided for each diagnosis. Despite these interventions, the patient's clinical condition continued to deteriorate, leading to death. This underscores the difficulties in early MVD diagnosis and highlights the need to consider MVD in the differential diagnosis of febrile illnesses in endemic regions, particularly when standard treatments do not lead to improvement [12].

MVD can cause severe hemorrhage, which involves bleeding under the skin, into the body cavities and internal organs [2]. In this case, ecchymosis, purpura, and petechiae were observed in various internal organs, with extensive hemorrhagic effusion of the body cavities and ecchymosis of the external body parts. This extensive vascular leakage aligns with the widespread and severe effects of MVD on the blood clotting cascade and the vascular system [1]. MVD is a severe hemorrhagic fever with high mortality rates that affects various organ systems and causes severe bleeding, DIC, and multiorgan dysfunction [13]. Our case showed edema, bleeding, and consolidation of the lungs, suggesting acute respiratory distress syndrome, a common complication of MVD [14]. These pulmonary findings explain the patient's clinical presentation of worsening hypoxia, requiring high-flow oxygen therapy. Moreover, our case showed a pale-yellow and hemorrhagic liver along with hyperemia of the gallbladder mucosa, suggesting acute liver failure, which is typical of MVD [15]. This correlates with the slight increase in liver enzyme levels and yellowish discoloration of the conjunctiva noted in the patient's clinical history. The autopsy also revealed an enlarged, dark red, friable spleen, which indicates significant involvement of the reticuloendothelial system in the disease process. Moreover, the presence of blood in the stomach and hyperemia of the mucosal lining support the gastrointestinal symptoms experienced by the patient, including vomiting and diarrhea. The congestion and hemorrhage observed in the pancreas and kidneys further demonstrate the multiorgan involvement characteristic of MVD[10,16]. In addition, the swollen appearance of the brain with blood-tinged effusion in the ventricles suggests cerebral edema and potential neurological involvement, which could explain the patient's clinical history of confusion immediately before death.

Nonetheless, the manifestations of MVD can differ greatly among patients even during the same outbreak, although manifestations of febrile illness are commonly observed[4,17]. Kalungi et al. reported a case involving a patient with MVD who died 11 days after the onset of symptoms. Initially,

the patient exhibited symptoms of febrile illness, which later progressed to bloody stool and severe nasal bleeding and autopsy showed mild ascites and petechial hemorrhages in the subpleural areas of the lungs, with no evidence of hemorrhage in the skin or other organs[18]. This differs from our findings, which identified extensive hemorrhage in the skin, internal organs, and body cavities. The significant differences between these studies, particularly regarding the impact of MVD on internal organs and body cavities, are likely attributable to the Marburg virus strain, comorbidities, or individual immune responses[19,20]. Nonetheless, both studies shared similarities, as death was preceded by febrile illness symptoms with a similar duration from symptom onset to death, and hemorrhagic manifestations in the stomach.

This study offers essential insights into disease pathogenesis and the specific organ system effects of MVD, aiding the creation of targeted interventions. However, there are certain limitations to this study, such as the fact that the findings might not be relevant to all MVD cases, as it is a single case report, and the inability to understand the microscopic changes of the disease due to biosafety concerns of performing histopathological examinations.

In summary, this autopsy case report sheds light on the pathological features of MVD and deepens our understanding of its severe systemic characteristics. Autopsy results offer a detailed perspective on the systemic impact of MVD, aligning closely with the patient's clinical symptoms and disease progression. The extensive hemorrhagic signs, involvement of multiple organs, and vascular damage noted in this case align with the established pathophysiology of MVD and other viral hemorrhagic fever[21].

Conclusion

This case report provides valuable insights into the autopsy findings of a patient with MVD and contributes to our understanding of this rare and highly infectious disease. The key findings include widespread ecchymoses, petechiae, and purpura on both external and internal surfacesand evidence of multiorgan involvement. This study highlights the challenges in the early diagnosis of MVD, and emphasizes the importance of considering MVD in the differential diagnosis of febrile illnesses in endemic areas.

Although this case report may not be applicable to all instances of MVD, it shares significant role in expanding the limited autopsy-based literature on MVD. Future investigations should aim to conduct more extensive autopsy studies incorporating histopathological analyses across a larger sample size to better understand the disease and guide the development of targeted interventions. Additionally, the disposal of histological and toxicological samples before analysis in line with biosafety protocols underscores the importance of following safety measures in handling MVD cases, which is vital for preventing the spread of this highly infectious disease.

Abbreviations

MVD- Marburg virus disease

DIC- disseminated intravascular coagulation

RT-PCR- reverse transcriptase polymerase chain reaction

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Statements and declarations:

Ethical approval: The outlined study protocol for this case report obtained ethical approvalon the date of July 20, 2025, reference number 005/2025 from the research project committees operating within the Rwanda Forensic Institute (RFI).

Informed consent: This study is a case report and informed consent for the study was obtained from the family of the deceased.

Consent to Publish declaration: Informed consent was obtained from the deceased's family in this study for the article to be published.

Compliance with ethical standards: The study was carried out following the ethical standards of the Declaration of Helsinki (Finland).

Conflict of interest: Payment/servicesinfo: no financial support was received from any organization for this study.

Financial relationships: there is no financial relationships at present or within the previous three years with any organizations that might have aninterestinthis study.

Other relationships: there isnoother relationships or activities that could appear to have influenced this study.

Data availability: Not applicable.

Clinical trial number: Not applicable.

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