Lassa fever – full recovery without ribavarin treatment: a case report

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Abstract

Background: Lassa fever is a rodent-borne zoonosis that clinically manifests as an acute hemorrhagic fever. It is treated using ribavarin. Surviving Lassa fever without receiving the antiviral drug ribavarin is rare. Only few cases have been documented to date.

Case Presentation: We report a case of a 59-year old female with fever who was initially thought to have acute pyelonephritis and sepsis syndrome with background malaria. Further changes in her clinical state and laboratory tests led to a suspicion of Lassa fever. However at the time her laboratory confirmatory test for Lassa fever returned, her clinical state had improved and she made full recovery without receiving ribavarin. Her close contacts showed no evidence of Lassa virus infection.

Conclusion: This report adds to the literature on the natural history of Lassa fever; and that individuals may survive Lassa fever with conservative management of symptoms of the disease and its complications.

Keywords: Lassa fever; viral hemorrhagic fever, survival, ribavarin

DOI: http://dx.doi.org/10.4314/ahs.v14i4.40

Introduction

Lassa fever is a zoonotic disease that commonly manifests as an acute viral hemorrhagic fever. It was first described in northeastern Nigeria in 1969, and it is endemic in West Africa. The animal reservoir of the Lassa fever virus is a rat, Mastomys natalensis. Transmission occurs through direct exposure to the excreta/blood of infected rats, or from person to person via body fluids. The incubation period ranges between 7 to 18 days. In endemic areas, an estimated 300,000 – 500,000 cases and 5000 to 10,000 deaths occur annually. About 80% of persons infected with the Lassa virus are asymptomatic; but in the remaining 20%, the illness manifests as a febrile illness of variable severity associated with multiple organ dysfunctions with or without hemorrhage.

Since the discovery of Lassa fever, Nigeria has experienced several epidemics; one of the most recent affected 19 States of the federation includes Ebonyi State. Majority of the earliest cases of Lassa fever died. Only one of these early laboratory confirmed case was documented to have survived with supportive therapy alone. Early attempts at treating Lassa fever involved total isolation and supportive therapy with or without the use of the convalescent serum or antibody. Presently, Lassa fever management involves the use of ribavarin, supportive therapy, and simple barrier nursing usually in a specific ward dedicated for the disease. Treatment with intravenous ribavarin is particularly useful in decreasing Lassa fever mortality – its administration within the first 6 days of illness has been shown to decrease the mortality of severe Lassa fever from 55% to 35%.

We recently encountered an individual with Lassa fever that survived without receiving ribavarin. At Lassa fever suspicion, the patient’s clinical management was based on the World Health Organisation (WHO) / Centers for Disease Control (CDC) guidelines. However, at the time her laboratory confirmatory test for Lassa fever returned, her symptoms had markedly resolved; she was not given ribavarin but monitored closely and discharged.

Case presentation

The patient was a 59 year old female farmer who hails and resides in Ebonyi State, Nigeria. She was admitted with a one week history of fever, shaking chills, severe headaches, anorexia and body weakness. On the day of presentation, she had two episodes of vomiting but no hematemesis. She admitted to taking meals of game that often included rat meat. Before presentation, she visited a district hospital where she was treated with intravenous quinine and chloramphenicol and at presentation she was on oral antimalarials (artemether-lumefantrine) and ciprofloxacin without improvement. She was a known hypertensive diagnosed three years ago; and had been compliant with her anti-hypertensives.

On examination, she had a temperature (T) of 39.1°C and was moderately pale; pulse rate was 78 beats per minute and blood pressure 130/80 mmHg. Her respiratory rate was 32 cycles per minute; other components of the chest and neurologic examinations were unremarkable. On abdominal examination, she had hepatomegaly and bilateral loin tenderness. A diagnosis of acute pyelonephritis and sepsis syndrome with background poorly treated malaria was made. Blood samples were collected for blood culture, complete blood count and film for malaria parasites, serum electrolytes, urea and creatinine, hepatic enzymes, urinalysis and urine microscopy, culture and sensitivity. She continued her oral antimalarials, antibiotic, and antihypertensives as well as intravenous fluid infusion. Her urinalysis showed massive hematuria (++++), proteinuria (+++), glucose (+), bacteruria (+) and granular cast (+++). The blood examination showed malaria parasitaemia (+), leucopenia with relative lymphocytosis (Table 1).

Table 1: Complete blood count changes in an individual with confirmed Lassa fever

<table>
<thead>
<tr>
<th>Variables</th>
<th>Day 1</th>
<th>Day 4</th>
<th>Day 8</th>
<th>Day 11</th>
<th>Day 15</th>
<th>After 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>12</td>
<td>8.3</td>
<td>9</td>
<td>9.3</td>
<td>9.6</td>
<td>10</td>
</tr>
<tr>
<td>WBC count</td>
<td>1.7</td>
<td>4.2</td>
<td>4.4</td>
<td>6.0</td>
<td>6.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>48</td>
<td>16</td>
<td>13</td>
<td>30</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>52</td>
<td>84</td>
<td>84</td>
<td>70</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0</td>
<td>02</td>
<td>01</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0</td>
<td>0</td>
<td>02</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Basophils</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytes</td>
<td>80</td>
<td>62</td>
<td>102</td>
<td>130</td>
<td>149</td>
<td>-</td>
</tr>
<tr>
<td>Malaria parasite</td>
<td>(+)</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>-</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>0.6</td>
<td>1.3</td>
<td>1.4</td>
<td>-</td>
<td>-</td>
<td>0.2 – 2.0</td>
</tr>
</tbody>
</table>
survival of other patients with Lassa fever. It suggests that conservative management of symptoms and the disease and its complications may improve survival of individuals infected with Lassa fever. There is need for the development of reliable point of care tools in order to quickly confirm or rule out the diagnosis of Lassa fever, and other viral hemorrhagic fevers once suspected. This is the next challenge in tackling Lassa, Ebola, and Marburg hemorrhagic fevers in Africa.

Conflict of interest statement:
The authors have no conflict of interest to declare.

Funding:
No specific funding was received for the study.

Acknowledgement:
We thank Prof Stephan Grüter of the Department of Virology, Bernhard-Nocht-Institute, Germany for performing the confirmatory laboratory test. The Department of Virology of the Bernhard-Nocht-Institute is a WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and Research.

References:

Also, her serum hepatic enzymes were elevated (aspartate aminotransferase, 101 IU per liter; alanine aminotransferase, 68 IU per liter). However, blood culture, serum bilirubin, urea and creatinine were unremarkable.

Three days later, the fever persisted (T, 39°C), and she developed noisy breathing. On examination, she had coarse cradles at her lung bases, and rhonchi over all her lung zones. The oral antibiotics were stopped and she was commenced on intravenous amoxicillin-clavulanic acid, and later ceftazidime, and intravenous aminosu- rate. On the 8th day of admission, she still had fever (T, 38.2°C), but no longer had joint pains and headaches. A repeat CBC showed anaemia, neutropenia, massive lymphocytosis and thrombocytopenia (Table 1); how- ever, malaria parasites were absent. The Lassa fever management team was invited. Following review, a di- agnosis of suspected Lassa fever was made. The patient blood sample was sent for Lassa virus-specific reverse transcriptase polymerase chain reaction (RT-PCR) using previously described methods.

Over the next three days, she had a gradual fall in tem- perature. On the 11th day of admission, she complained of numbness on her feet, and her temperature had fall- en to 37.4°C. The noisy breathing and abdominal pain has resolved. On that day, her Lassa virus-specific RT- PCR test results returned and the diagnosis of Lassa fever was confirmed. Due to her improving clinical state, intravenous ribavirin was not commenced; but her temperature was monitored closely. The intrave- nous antibiotics were continued with oral vitamin B-complex. The numbness resolved on the 14th day of admission. Two repeat CBC done on the 11th and 15th day of admission showed improving indices (Table 1). The patient was discharged on the 18th day of admission. On follow-up visits two and four weeks after dis- charge, she remained well. A CBC done two weeks after discharge showed further improving hematologic indi- ces (Table 1). Presently, she has a monthly follow-up appointment.

Sixteen individuals found to be high-risk contacts of the patient were screened but showed no evidence of Lassa virus infection.

Discussion:
Surviving Lassa fever without antiviral treatment using ribavirin is perceived to be rare. Only one individual has been documented to have survived without receiv- ing the anti-viral agent ribavirin. Others, who had sur- vived without receiving ribavirin were not confirmed, and if confirmed, were either given serum of the Lassa fever survivor1, or had scanty information on how they were managed. At presentation, our patient's signs and symptoms were insufficient to consider a differential diagnosis of “suspected Lassa fever”2. But, given that she still had malaria parasitaemia and bacteruria, Lassa fever suspicion was given less consideration. However, the persistence of severe fever despite receiving various antiinflammatories and antibiotics as well as evidence of clearance of the malaria parasitaemia reignited the sus- picion of Lassa fever. The first documented survivor of Lassa fever also received empirical antiinflammatories and antibiotics despite no evidence of bacteria or plasmomi- um infection3. It is possible that these agents may have some effect on the pathophysiology of Lassa fever.

At the time of the confirmation of Lassa fever, the pa- tient’s clinical state had substantially improved; hence ribavirin was not given to her. Moreover, the patient had features that are known adverse effects of ribavirin; anaemia, rigors, nausea and vomiting, abdominal pain, fatigue, and headache39, were key symptoms the patient presented with. If ribavirin was administered and her clinical state deteriorates, it will be difficult to differenti- ate between the adverse effects of ribavirin and wors- ening of the Lassa fever. The Lassa virus-specific RT- PCR used to confirm the diagnosis is the gold standard for Lassa fever confirmation. Also, the RT-PCR assay currently in use in Nigeria has 100% sensitivity in de- tecting the local strains of the Lassa virus3. She had an admission AST ≥ 150 IU per liter, a previous study has shown that hospitalized Lassa fever cases with ad- mission AST ≥ 150 IU per liter have increased mortal- ity4. Our report suggests that a patient with laboratory confirmed Lassa fever with falling temperature, low ad- mission AST <150 IU per liter and improving clinical state may not require treatment with ribavirin.

None of the individuals classified as a high-risk contact of the patient had evidence of Lassa virus infection. Also, none of the health workers who participated in the management of the patient were infected. This agrees with previous findings that Lassa virus is not as infec- tious as it is always suspected—previous observations have shown that even repeated, often intimate contact of Lassa fever patients described by family members often fail to transmit the infection11,12. It was not pos-