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 ribavirin. Surviving Lassa fever without receiving the antiviral drug ribavirin 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 ribavirin. 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

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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.1 The animal reservoir of the Lassa fever virus is a rat, Mastomys natalensis. Transmission occurs through direct contact to the excreta/blood of infected rats, or from person to person via body fluids. The incubation period ranges between 7 to 18 days.2 In endemic areas, an estimated 300,000 – 500,000 cases and 500 to 10,000 deaths occur annually.3 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.4 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.5 Majority of the earliest cases of Lassa fever died.6 Only one of these early laboratory confirmed case was documented to have survived with supportive therapy alone.1 Early attempts at treating Lassa fever involved total isolation and supportive therapy with or without the use of the convalescent serum or antibody.5-6 Presently, Lassa fever management involves the use of ribavirin, supportive therapy, and simple barrier nursing usually in a specific ward dedicated for the disease.4 Treatment with intravenous ribavirin 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 5%.7

We recently encountered an individual with Lassa fever that survived without receiving ribavirin. At Lassa fever suspicion, the patient’s clinical management was based on the World Health Organisation (WHO) / Centers for Disease Control (CDC) guidelines.8 However, at the time her laboratory confirmatory test for Lassa fever returned, her symptoms had markedly resolved; she was not given ribavirin 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 chloroquine 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>02</td>
<td>0</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>Positive (+)</td>
</tr>
<tr>
<td>Reticulocyte</td>
<td>-</td>
<td>0.6</td>
<td>1.3</td>
<td>1.4</td>
<td>-</td>
<td>0.2 – 2.0</td>
</tr>
</tbody>
</table>

We all express our gratitude to the patient for her consent and cooperation during her stay in our hospital.
transcriptase polymerase chain reaction (RT-PCR) was used to confirm the Lassa fever diagnosis. The patient also had malaria parasites, which were absent. A repeat CBC showed anaemia, neutropenia, and massive lymphocytosis and thrombocytopenia. The patient's symptoms were insufficient to consider a differential diagnosis of suspected Lassa fever. But, given that she still had malaria parasitaemia and bacteriuria, Lassa fever suspicion was given less consideration. The persistence of severe fever despite receiving various antimalarials and antibiotics as well as evidence of clearance of the malaria parasitaemia suggested the suspicion of Lassa fever. The first documented survivor of Lassa fever also received empirical antimalarials and antibiotics despite no evidence of bacteria or plasmmodium infection. 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 patient'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 headache. Key symptoms the patient presented with if ribavirin was administered and her clinical state deteriorates, it will be difficult to differentiate between the adverse effects of ribavirin and worsening of the Lassa fever. The 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 intravenous 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 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.

None of the individuals classified as a high-risk contact of the patient had evidence of Lassa virus infection. None, also 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 infectious 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 infection.11,12 It was not possible to demonstrate other changes in the patient's biochemical parameters during recovery and discharge due to high treatment costs.

Future research needs to be conducted in communities with Lassa fever to identify individuals with high circulating immunoglobulin-G antibodies to the Lassa virus i.e., those who might have had clinical or subclinical infection and recovered. Identified cases needs to be evaluated to determine the factors associated with survival. Furthermore, they should be followed in a cohort study to determine if past infection with Lassa virus affects the risk of recurrence, re-infection, or clinical presentation of other diseases which manifests with fever.

Conclusion

This report adds to the literature on the natural history of Lassa fever. It suggests that conservative management of symptoms of 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.4

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References