Lassa Fever Case Report: Challenges In Making Early Diagnosis

ABSTRACT

Introduction: Lassa fever is a disease of public health importance because of the associated morbidity as well as high case fatality rate in patients admitted to hospital. Even after recovery, there may be residual problems such as sensorineural hearing loss. The initial presentation of Lassa fever may be with non-specific symptoms similar to what is seen in the more common febrile illnesses such as malaria. In such a setting therefore, early recognition of Lassa fever may be difficult. **Case Presentation:** We report a case of Lassa fever that presented to our institution. She was a middle aged woman who had non-specific symptoms of febrile illness and who died in less than 48 hours of admission. She had a subtle bleeding on the lip just before death which was what raised the suspicion for Lassa fever. Diagnosis of Lassa fever was confirmed retrospectively. **Conclusion:** When the presenting symptoms are non-specific, a high index of suspicion is required for early recognition of Lassa fever. Early diagnosis is important for early intervention with ribavirin as well as for limiting the spread of the disease.

Keywords
Lassa fever, Lassa virus, Lassa fever diagnosis, Lassa fever symptoms and signs

INTRODUCTION

Although Lassa fever is endemic in Nigeria, as in some other West African countries (Richmond et al. 2003), it is not as common in Nigeria as other febrile illnesses such as malaria and typhoid fever. Even in the same country, there is a geographical variation in the incidence of Lassa fever (WHO 2020). When the initial presentation of Lassa fever is with non-specific symptoms similar to those of more common febrile illnesses, early recognition of Lassa fever may be difficult in places where malaria is very common and Lassa fever is rare. The first challenge arising from not making early diagnosis of Lassa fever in a patient is that appropriate intervention may not be instituted early enough and it is well known that clinical outcome in Lassa fever is improved by early intervention with ribavirin in addition to supportive care (Richmond et al. 2003). The second challenge arising from not making early diagnosis is that adequate prevention protocols may not be followed by the health care workers attending to the patient in order to prevent secondary transmission. In Nigeria, diagnostic tests for Lassa fever are available only in five centers distributed all over the country (WHO 2020). Depending on the distance between the attending hospital and the diagnostic center, and also on the demand on the diagnostic center which is seasonal, there may be some delay in confirming or ruling out a suspected case of Lassa fever.

Up till December 31st, 2019, no case of confirmed Lassa fever had been reported from the Enugu State University of Science and Technology Teaching Hospital, Parklane, Enugu, Nigeria. Between January 2020 and February 2020, the first two cases of Lassa fever presented within a space of five weeks of each other to this hospital. The two patients died. However, no health worker was infected even though the diagnosis of Lassa fever was not made early enough. The second of the two cases is presented in this case report in order to highlight the challenges in making early diagnosis of Lassa fever.

CASE REPORT

On the 18th of February, 2020, a 56 year old female Nigerian who was residing in a suburb near the state capital of Enugu State was referred to our institution when her health condition did not improve following initial treatment. She gave a history of fever and generalized body weakness of a week duration, and difficulty in breathing and abdominal pains of three days duration. The fever was of high grade, intermittent, worse at night and associated with chills and rigors. There was no history of vomiting, diarrhea or bleeding from any part of the body. There was no history of cough, neck pain, pain on passing urine or sore throat. She was not a known hypertensive or diabetic. She first went to a private hospital where she was admitted and treated without improvement before the referral.

At presentation, her radial pulse was 100 beats per minute, respiratory rate was 28 cycles per minute and blood pressure (BP) was 80/50 mmHg in the supine position. Temperature was sub normal. An initial working diagnosis of malaria to rule out enteric fever was made by the Accident and Emergency Medical Officer(Casualty Officer) who commenced her on intravenous fluids (normal saline initially and subsequently alternated normal saline with 5% Dextrose water), treatment for malaria and intravenous ceftriaxone 1gm twice daily as empirical treatment for typhoid fever, pending laboratory investigations.

She was subsequently reviewed by the medical team on call. Physical examination revealed a middle aged woman who was tachypnoeic, afebrile, and had no cyanosis, no digital clubbing, no jaundice and no pedal edema. The respiratory rate was now 30 cycles per minute and her chest was clinically clear. By this time her BP had improved to 100/60mmHg. The apex beat was at the 5th left intercostal space in the midclavicular line. The abdomen showed generalized tenderness with guarding. Liver, spleen and kidneys were not palpable. A working diagnosis of typhoid fever was made. Intravenous metronidazole and analgesic were added to her drug regimen. The following laboratory investigations were to be done. Full blood count, erythrocyte sedimentation rate (ESR), blood smear for malaria parasites, fasting blood glucose, widal test, serum electrolytes, urea and creatinine, urinalysis and urine microscopy, culture and sensitivity, stool microscopy, culture and sensitivity, blood cultures, chest X-ray and abdominal ultrasound examination.

Less than 48 hours after the patient presented at the hospital, blood was noticed around her lips. Her condition deteriorated rapidly and she died despite resuscitative measures.

The infectious disease prevention and control team was informed. The patient's blood samples which were earlier collected for basic laboratory investigations were retrieved from the laboratory and sent for Lassa virus test and the resultant reverse transcription polymerase chain reaction was positive. The team also commenced contact tracing. There was no evidence of secondary transmission from the index patient to the hospital workers or to other contacts traced.

DISCUSSION

The Reported Case

We reported a case of a middle aged woman who presented with non-specific symptoms of febrile illness in a center where malaria and typhoid fever are more common and Lassa fever is rare. She died in less than 48 hours of admission. This patient was seen before the arrival of COVID-19 in Nigeria. The first case of COVID-19 in Nigeria was an Italian citizen who flew into

Lagos from Milan on February 25th, 2020 (The Guardian. 2020), while the first reported two cases of COVID-19 in Enugu State was on 27th March, 2020. The patient in this case report had never travelled out of Nigeria. She had had no contact with anybody from outside the country, at least, in recent times. She was a farmer living in a suburb. Therefore, the possibility of COVID-19 as a differential diagnosis was very unlikely. Multidrug resistance by malaria parasites is a problem in this part of the world. *Plasmodium falciparum* is the commonest malaria parasite in Nigeria (WHO 2019), and it is one of the two species of malaria parasites notorious for multidrug resistance (CDC 2020). Therefore, even if non-specific symptoms persists in a patient after malarial therapy, it still may not rule out the possibility of the person having malaria. Other authors have highlighted the difficulty in making diagnosis of Lassa fever (Richmond et al. 2003), (Amorosa et al. 2010), (Ibekwe 2012).

Although, the patient had fever in the early stage of her illness, fever was not prominent when she presented to our hospital and she was not febrile on examination. Bleeding which is considered to be a classical feature of Lassa fever, as in other viral haemorrhagic fevers, was subtle and a terminal event in this patient. A little bleeding was noticed around her lip just before death which was what raised the suspicion for Lassa fever. In one case-control study in Sierra Leone, mucosal bleeding occurred only in 17% of cases of Lassa fever patients (McCormick et al. 1987). Until the time bleeding was noticed in our patient, she was treated like any other patient rather than like a high risk patient. Fortunately, there was no secondary transmission to any hospital staff from this index case. This case illustrated some of the challenges faced by clinicians in this part of the country in making early diagnosis of Lassa fever. It also showed the potential health risks to health staff and to others when such diagnosis is not made early enough. This was the second case of Lassa fever seen in this hospital. Enugu State has a very low incidence of Lassa fever. So far this year, there have been only 10 confirmed cases of Lassa fever in Enugu State compared to 339 confirmed cases in Edo State and 363 confirmed cases in Ondo State (NCDC 2020a).

An Overview of Lassa Fever

Lassa fever, a disease of public health importance, is one of the viral haemorrhagic fevers. It is caused by Lassa virus which is an arenavirus transmitted by *Mastomys natalensis* either directly by eating rat or by taking food contaminated by rat's urine or faeces (Richmond et al. 2003), (WHO 2020). Lassa fever is endemic in Nigeria and in some other West African countries such as Guinea, Benin, Mali, Ghana and Sierra Leone and Senegal (Richmond et al. 2003). There is seroprevalence evidence of human exposure to Lassa fever virus in some of the central African countries like Central African Republic and Democratic Republic of the Congo (Richmond et al. 2003). Also, there have been reports of imported Lassa fever to other continents of the world (Kitching et al 2009), (Amorosa et al 2010). Although, majority of subjects (about 80%) with Lassa fever may have no symptoms (WHO 2020), in those on admission, the case fatality rate may be as high as 28% (Inegbenebor et al 2010).

The period from January 2020 to February 2020 when the first two cases of Lassa fever presented to this hospital fell within the dry season when the incidence of Lassa fever usually peaks (WHO 2020). Between 1st January 2020 and 16th August, 2020, there were a total of 1061 confirmed Lassa fever cases in Nigeria with 222 deaths (NCDC 2020a). For comparison, estimated 100 million malaria cases occur yearly in Nigeria with estimated 300,000 deaths (Nigeria Malaria Fact Sheet 2020), indicating that malaria is by far a more common disease in Nigeria than Lassa

fever. For the year 2020, the emergency phase for Lassa fever in Nigeria lasted from 24th of January 2020 to 28th of April, 2020, which also falls within the dry season.

Laboratory tests for Lassa fever include enzyme linked immunosorbent assay (ELISA), indirect fluorescent-antibody test (IFA), virus isolation and reverse transcription polymerase chain reaction (RT-PCR) (Niklasson et al. 1984), (Bausch et al. 2000). Each test has its own sensitivity and specificity (Bausch et al. 2000). Virus isolation and reverse transcription polymerase chain reaction are considered to be the gold standard (Bausch et al. 2000). In Nigeria, test for Lassa fever are available in five centers distributed all over the country (WHO 2020).

A number of complications can occur in Lassa fever, of which one of the disabling complications is sensorineural hearing loss. In a study done in Sierra Leone [Richmond et al. 2003], a high incidence of sensorineural hearing loss was found among those suffering from Lassa fever. Sensorineural hearing loss was also found among those with serological evidence of past expose to Lassa fever virus (Richmond et al. 2003), indicating that hearing loss may persist in some people even after recovery from Lassa fever.

Management of Lassa fever patients remains a major occupational risk for health workers. In 2020 (WHO 2020) as in previous years, there have reported Lassa fever cases as well as reported Lassa fever related deaths among health workers. Early recognition of Lassa fever cases is important for minimizing secondary infection to health workers.

Challenges in making early diagnosis of Lassa fever

Due to the non-specific nature of the symptoms of Lassa fever in the early stage of the disease, the first thing a patient in malaria-endemic zone will think of is malaria and he may resort to self-treatment for malaria. Because in most cases, the patient may not have any symptoms, (WHO 2020), the Lassa fever may go unnoticed. Even when the patient is symptomatic, he may visit a private medical laboratory for laboratory tests and treatment unrelated to Lassa fever, and this is a common practice in this part of the world. The two cases that presented to this hospital were brought in when the patients became very ill.

Apart from late presentation of patients to centers which has the capability of managing cases of Lassa fever, delay in getting a laboratory test may be another cause of delay in confirming or ruling out a suspected case of Lassa fever. If diagnosis is made early enough, therapeutic intervention with ribavirin can be made early. Starting ribavirin early (within the first six days) in addition to supportive care improves clinical outcome in Lassa fever (Richmond et al. 2003). Intravenous ribavirin is preferred to oral ribavirin for the same reason (Richmond et al. 2003). Also, not recognizing a case of Lassa fever may cause a delay in deploying adequate prevention protocols aimed at limiting the spread of the disease to health care workers, to other patients as well as to patients' relatives. And this include proper handling of the patient's body fluids including laboratory samples.

Conclusion and Recommendation

A very high index of suspicion is required to be able recognize a case of Lassa fever in a place where malaria and other febrile illnesses are common and Lassa fever is rare. Late presentation of Lassa fever patients to centers capable of managing cases of Lassa fever still remains a major

challenge. Early diagnosis of Lassa fever is important for timely institution of definitive therapy as well as for containment of the disease.

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