THE FIRST CASES OF LASSA FEVER IN GHANA

E.K. DZOTSI[1], S-A. OHENE[2], F. ASIEDU-BEKOE[3], J. AMANKWA[4], B. SARKODIE[1], M. ADJA-BENG[1], A.M. THOUPHIQUE[5], A. OFEI[3], J. ODURO[3], D. ATITOGO[3], J.H.K BONNEY[6], S.C.N. PAINTSIL[6] and W. AMPOFO[6]

[1]Disease Surveillance Department, Ghana Health Service, Accra, Ghana, [2]World Health Organization Ghana Country Office, P. O Box MB 142,Accra, Ghana [3]Ashanti Regional Health Directorate, Ghana Health Service, P.O. Box 1908, Kumasi, Ghana [4]Public Health Directorate, Ghana Health Service, Accra, Ghana [5]Manso-Nkwanta Health Centre, Amansie West District, Nkwanta ,[6]Noguchi Memorial Research Institute for Medical Research, University of Ghana, P.O. Box LG 581, Legon, Ghana

Corresponding Author: *Dr. Sally-Ann Ohene* ***E-mail address:*** *salohene@yahoo.com*

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SUMMARY

Lassa fever is a zoonotic disease endemic in West Africa but with no previous case reported in Ghana. We describe the first two laboratory confirmed cases of Lassa fever from the Ashanti Region of Ghana detected in October and December, 2011.

Keywords: Lassa fever, viral haemorrhagic fever, *Mastomys*

INTRODUCTION

Lassa fever (LF) is an acute viral haemorrhagic illness that is caused by an arenavirus.[1] It is named after Lassa, the town in Nigeria where the cases were first identified [1]. It is a zoonotic disease, with the animal reservoir reported as the rodent Mastomys natalensis[2]. See Figure 1.

Figure 1 *Mastomys natalensis*
Source: Shirley Nimo-Paintsil, picture taken at Mangoase, Kintampo South District, 7 August, 2011

Humans become infected through aerosols, direct contact with urine or droppings of infected rodents or direct contact with blood, pharyngeal secretions, urine and other body secretions of an infected person.[1, 2]

The incubation period is 6 to 21 days. The onset of LF illness is gradual, with non-specific signs and symptoms starting with fever, general weakness and malaise. After a few days, headache, sore throat, muscle pain, chest pain, vomiting, diarrhoea and abdominal pain may follow. Severe cases may progress to show facial swelling, bleeding from mouth, nose, vagina or gastrointestinal tract, and low blood pressure.

Shock, seizures, disorientation, and coma may be seen in the late stages. Deafness occurs in 25% of patients but half recover some function after 1-3 months. Transient hair loss and gait disturbance may occur during recovery[1, 2, and 3]. About 80 % of LF infections are mild or asymptomatic. The overall case fatality rate (CFR) is reported as1%; however CFR among patients hospitalized for LF is about 20%[3].

LF occurs in all age groups in both men and women[3] and is known to be endemic in Guinea, Liberia, Sierra Leone and parts of Nigeria[1]. The burden of Lassa fever is estimated to be 300,000 to 500,000 cases with about 5,000 deaths occurring annually in West Africa.[1,2] Despite the endemicity of LF in neighbouring countries, there have been no previous reports of LF infection in Ghana.

These first two cases were from Manso-Nkwanta in Amansie West District of Ashanti Region shown in the map in Figure 2.

Case 1

A 19 year old male farmer, hunter, trader in game meat, illegal surface miner and a resident of Essuminya community (Global Positioning System, GPS) coordinates: N $06^0$27.941 W $001^0$54.169) in Manso-Nwanta sub-district of the Amansie West District, Ashanti Region presented at the Manso-Nwanta Health Centre (MNHC), on 12th October 2011, at 12.15p.m with fe-

ver, chills and joint pain of 3 days duration. A day before the onset of illness, the man went hunting with 2 other household members.

Figure 2 Map of Ghana showing Amansie West District (AWD)
Source: *http://mapsof.net/map/un-ghana*

That evening they had a meal of game that included rat meat. The patient had not travelled outside the community in the preceding 21 days. Initial physical examination revealed that he was fully conscious, not pale, not jaundiced, but febrile with temperature of 39.5^0C. Blood pressure was 120/60 mm Hg and his pulse was 120 beats per minute. The respiratory rate was 86 per minute. Initial laboratory results showed haemoglobin of 9.8g/dl, white cell count of 11.3 $x10^9$/L and malaria parasites (+). An initial diagnosis of severe malaria with differential of septicaemia was made. The patient was admitted the same day in the general ward with other patients.. He was initially treated with start doses of intravenous (IV) Quinine 600mg, intramuscular Diclofenac 75mg, intravenous dextrose infusion 500 mls and tepid sponging.

About 2 hours following admission (at 2.05 pm) the Clinical Nurse In-Charge of the Health Centre was called to review the patient as he had developed muscle cramps, palpitations, delirium and bleeding from the nose, ears, mouth and anus. A diagnosis of Viral Haemorrhagic Fever (VHF) was suspected and the patient was started on one litre of IV normal saline infusion and Haemacel 500mls.

While considering referral to the nearest hospital, (Agroyesum Hospital or Komfo Anokye Teaching Hospital), the patient died at 2.26 pm the same day.
The body was immediately put in a coffin and sealed at the MNHC under supervision of the District Director of Health Services. Strict observations and adherence to infection prevention and control measures were undertaken. The deceased was buried at the public cemetery in the outskirts of Essuminya community under police protection due to community agitation against the non-release of the body for traditional funeral rites.

Venous blood, which had been taken from the patient, was sent to the National Public Health Reference Laboratory (NPHRL), Accra on the 13th of October 2011. An initial laboratory test at the NPHRL was negative for Yellow Fever (YF) IgM. The blood sample was subsequently sent to Noguchi Memorial Research Institute for Medical Research (NMIMR) for further testing for typical VHFs.

Application of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) testing based on methods by Demby A. et al.[4] confirmed the presence of Lassa fever virus in the blood sample on 21 October 2011 at the NMIMR. Other RT-PCR tests following methods as reported by Pierre V. et al.[5] for other VHFs such as Ebola, West Nile Fever, Marburg, Dengue haemorrhagic fevers were negative. Blood samples from 20 contacts of the patient (defined as persons who had slept in the same household as the case, had direct physical contact with him or touched his linen or body fluids) were also subjected to RT-PCR tests and found to be negative for Lassa fever and the other VHFs.

Case 2

The second case was a 24 year old male farmer, mason, and a resident in Manso Nkwanta which is 5 km from Essuminya, the community that reported the first confirmed Lassa fever case (Case 1). He had no contact with the first case. He reported at the MNHC at11.20 pm on 3rd December 2011 with a day's history of productive cough with yellowish sputum, chest pain and fever. . He weighed 61kg, blood pressure was 134/48 mmHg and temperature was 38.7^0C. He was dyspnoeic, febrile and pale but not jaundiced. He had bilateral crepitations.

The initial diagnosis was bilateral Lobar Pneumonia. Laboratory investigations indicated a white cell count of 17.1 $X10^9$/l and haemoglobin of 6.1g/dl. No malaria parasites were seen on blood film. The patient was detained at MNHC and managed with IV Crystalline Penicillin 4 mega units 6 hourly, IV Gentamicin 80mg 8 hourly, IV Ceftriaxone 1g 12 hourly, 2 tablets of

Paracematol orally, IV 500 ml Normal Saline, IV 5% Dextrose 500 ml, and IM Quinine 600 mg 8 hourly.

Just about an hour after being detained, the Clinical Nurse was called to review the patient. The patient was vomiting blood and coughing with bloody sputum. The patient's condition worsened and he died 30 minutes following the review. A diagnosis of suspected VHF was made. Blood specimen was then collected and sent to the NPHRL on 5th December 2011. After a negative test for YF IgM, the blood sample was sent to the NMIMR where it was confirmed positive for Lassa fever virus by RT-PCR test (Demby A. et al.)[4] on 14th December 2011.

A review of his medical record revealed that he had earlier reported to the MNHC on 15th November 2011 with right ear pain, fever, chills and hyper salivation. He had a temperature of 39.1^0C at that time. A diagnosis of uncomplicated malaria to rule out sepsis was made. He was found to have malaria parasites (+) and his haemoglobin was 10.2 g/dl. He was admitted and treated with IV 5% Dextrose, IV Quinine, IM Diclofenac and IV Amoksiklav.

He was discharged on the 3rd day on oral Amoksiklav, oral Arthemether/Lumefantrine, multivitamins and Gentamicin ear drops. Relatives claim that after he was discharged from MNHC on 17th November 2011, he was well for about 4 days but relapsed and reported to another clinic at Poano in Bekwai Municipal on 22nd November where he was managed as a case of acute ear infection to rule out Tonsillitis. He was admitted for a day and then discharged. After that he had been apparently well until the night of 3rd December when he was rushed back to MNHC where he died.

DISCUSSION

The presentation of LF is varied and non-specific, often making clinical diagnosis difficult to distinguish from other diseases which cause fever, including malaria, shigellosis, typhoid fever, yellow fever and other VHF.[3] The first case described in this report presented with acute febrile illness with signs and symptoms typical for severe malaria and so with the confirmed presence of malaria parasites in the blood, was managed accordingly. This was the severe form as progression to bleeding and a severe sign was very rapid. The onset of illness and progression to the severe form of the second patient was more characteristic of classical LF.

The Ministry of Health/Ghana Health Service adapted and adopted the second edition of the WHO Integrated Disease Surveillance and Response (IDSR) Technical Guidelines in 2011. The second edition has a diagnostic entity of "Acute Haemorrhagic Syndrome/Acute Viral Haemorrhagic Fevers" with surveillance case definitions. Though a roll out training had not yet been carried out, sensitization and limited orientation of health workers had been done. This could have led to the high index of suspicion by the clinical nurse when the first patient's condition progressed to bleeding. With the second case, the onset of bleeding, reminiscent to the first case, possibly triggered the suspicion of LF. In both of these cases, the collaborative laboratory work between the NPHRL of the Ghana Health Service and the NMIMR led to the confirmation of these first Lassa fever cases in Ghana.

Ghana has not been reported to be endemic for LF so it is not surprising that it was not on the radar for differential clinical diagnosis. This is similar to the situation when the first case of LF was diagnosed from Mali.[6] Some studies have indicated the presence of antibodies to LF in serum samples from Ghana while other investigations in-country are ongoing.[7,8] There is also a previous report of an imported LF case into Germany from a patient who had a travel history to Ghana, Cote D'Ivoire and Burkina Faso.[9]

With the confirmation of LF in Ghana, the disease must now be considered among the differential diagnosis for febrile conditions particularly in areas where the *Mastomys* rodent is found. [3] A suspected case of LF is defined as an illness with gradual onset with one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia, chest pain hearing loss and a history of contact with excreta of rodents or with a case of Lassa fever.[10]

Laboratory confirmation of LF is by isolation of the virus or positive IgM serology or IgG seroconversion in paired samples or demonstration of Lassa antigen by immunohistochemistry or Enzyme Linked Immunosorbent Assay (ELISA) and a positive RT-PCR.[1-3]

The challenge however is that the definitive diagnosis requires testing that is available only in highly specialized laboratories.[3] Treatment of LF includes administration of Ribavirin and provision of supportive care. These cases indicate the need for increased awareness for LF. The virus is shed in the urine and droppings of the Mastomys and can be transmitted through direct contact with these materials, through touching objects or eating food contaminated with these materials, or through cuts or sores.[1]

Prevention at the community level involves preventing rodents from entering homes and storing grain and other foodstuffs in rodent-proof containers. Garbage should be disposed at secure sites far from homes with

the maintenance of clean environments.[2] Rodents should not be used as a food source.[3]

To reduce transmission of the disease through person-to-person contact or nosocomial routes, contact with patients' secretions should be avoided. Patients suspected to have LF should be cared for under specific "isolation precautions".

This includes the wearing of protective clothing such as masks, gloves, gowns, and face shields, and the systematic sterilization of contaminated equipment. Infected patients should be isolated until the disease has run its course. Contacts should be traced and follow up daily for 21 days. Blood samples should be taken for laboratory confirmation from contacts who develop any of the signs and symptoms described above Health care workers are at risk for contracting the disease as indicated in a nosocomial outbreak that occurred in February 2005 in Nigeria.[11] Therefore they should always ensure strict infection prevention measures including barrier nursing and isolation of Lassa fever patients. [12,13] The strict infection prevention measures taken during the burial of the deceased are commendable.

CONCLUSION

The first human cases of Lassa fever infection have been confirmed in the Amansie West District in Ghana and the possible source of infection was contact with rodents. These findings illustrate the need for clinicians and public health officials to remain alert to emerging infectious diseases such as Lassa fever. There is the need to develop preparedness and response plans that include the acquisition of appropriate logistics for diagnosis and management of VHFs including LF. Studies to identify the geographical prevalence of the host *Mastomys* rodent and determine the presence of LF in the animal are essential to determine the risk factors and geographical areas at risk for disease transmission in Ghana.

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