AN UNSUSPECTED YELLOW FEVER AND LASSA FEVER IN A TERTIARY HEALTHCARE FACILITY IN JOS, NORTH CENTRAL, NIGERIA: A CASE REPORT

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ABSTRACT

Background: Yellow Fever and Lassa Fever are both zoonotic diseases (Mosquito borne *flavirus* and Rodent borne *arenavirus*, respectively) and classified as viral haemorrhagic fevers (VHF) because of their common clinical presentations – especially fevers and bleeding during the terminal stages of the diseases. After an incubation period of 3 – 6 days in Yellow fever, and 2 – 21 days in Lassa fever: they present with fevers, rigors, headache, myalgia, nausea, and vomiting. Jaundice is noticed in Yellow fever, while Lassa in addition to other symptoms also present with sore throat (with patchy tonsillar exudate), dysphagia, dry cough, chest pain, and cramping abdominal pain, diarrhoea or epigastric pains. Gradual deterioration is associated with oedema of the face and neck, respiratory distress, pleural and pericardial effusions, encephalopathy, and haemorrhage from various sites (including hypotension and shock, nonrelated to blood loss).

The laboratory confirmation from a specialized virology laboratory was conducted for both disease conditions using reverse transcriptase polymerase chain reaction (PCR) testing, with containment facilities (biosafety level 4).

The management of each of these conditions is mainly supportive, although Ribavirin has significantly reduced mortality associated with Lassa fever; with best results obtained when drug is started early in the course of the illness. Reports of Yellow fever and Lassa fever co-infection are particularly scarce. The objective of this study was to report a successfully managed Case report in an Adolescent Child.

Case Report: A 10 – year old boy with a positive history of contact with and adult (grandmother) who died from a febrile illness, bleeding from body orifices and jaundice; presented with high grade fever, sore throat abdominal pain and passage of loose watery stool. All these symptoms were persistent for more than twelve days despite antibiotics and antimalarial medications. He was ill looking, febrile, anicteric and had right upper quadrant tenderness/hepatomegaly. A diagnosis of viral haemorrhagic fever was made, he was admitted and nursed in the isolation ward, infection prevention and control measures were observed, he had baseline investigations, supportive care and Ribavirin. PCR results was positive for Yellow fever and Lassa fever. He responded to treatment, was discharged home, and recuperated well during his follow up visits.

Conclusion: This case clearly illustrates the importance of having high index of suspicion following the significant history of contact with a probable case of viral haemorrhagic fever (absence of laboratory confirmation at the time of her death) by the index case, especially when there was non-response to routine treatment for common causes of fever in the community.

Key words: Yellow Fever, Lassa Fever, Viral Haemorrhagic Fever, Polymerase Chain Reaction.

INTRODUCTION

Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes.[1] Symptoms include headache, jaundice, muscle pain, nausea, vomiting and fatigue; a small proportion develop severe symptoms and approximately half of them die within 7 to 10 days.[1] Large epidemics (tropical areas of Africa and Central and South America) occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination.[1] Good supportive treatment in hospitals improve survival rates.[1] There is currently no specific anti-viral drug for Yellow fever.[1] Yellow fever is prevented by an extremely effective vaccine, which is safe and affordable.[1]

Lassa fever is an acute viral illness caused by the Lassa virus belonging to *Arenaviridae*; humans become infected from contact with infected animals.[2]Disease occurs throughout the year; though outbreaks occur during the dry season and early rainy season.[2]Approximately 80% of people who become infected with Lassa virus have no symptoms.[3] 20% of infections result in severe disease (general malaise, high fever, weakness, sore throat, headache, chest pain, cough, conjunctivitis, nausea and vomiting, diarrhea, swollen neck and face, bleeding, alteration of mental status), where the virus can cause multi-organ failure, sepsis and death.[3] While the overall case-fatality rate is estimated at 1%, observed case-fatality rate among patients hospitalized with severe cases of Lassa fever is 15% - 20% or higher.[3] High indices of suspicion in diagnosis and early goal directed therapy (Ribavirin and supportive care) is important.[3]Lassa fever outcome is good in the majority of patients, but remains an important cause of morbidity and mortality in endemic areas in Nigeria and other West African countries.[2]

VHFs prevalent in Africa comprises the *arboviral* infections Yellow fever, Rift valley fever, and Crimean-Congo haemorrhagic fever, the *arenaviral* infection Lassa fever and the *filoviral* infections Marburg virus disease and Ebola haemorrhagic fever.[4] The differential diagnosis of VHFs is extensive and based on other infections associated with features such as fever, rash, jaundice (other evidence of hepatic and renal involvement), haemorrhage from multiple sites (including needle, puncture wounds), leucopaenia, and thrombocytopaenia.[4] Accurate and rapid diagnosis of Yellow fever and Lassa fever is especially challenging due to the nonspecific clinical presentation, although reverse transcriptase PCR assays have been developed to diagnose all the VHFs. Confirmatory investigations should be carried out in a specialized virology laboratory with maximum containment facilities (biosafety level 4).[4]

Case Description

KH, a 10-year-old Tiv boy who presented with a two weeks history of fever, sore throat, abdominal pain and passage of loose watery stools. The fever was

high-grade intermittent and associated with chills and rigors. He also had sore throat with pain on swallowing, colicky abdominal pain and passage of loose watery and non-mucoid stools. There was no history of nausea, vomiting, haemoptysis, haematochezia or melaena. He had no history of dysuria, frequency, cough, chest pain, headaches, convulsions or loss of consciousness.

He was initially managed at a teaching hospital for Typhoid and Malaria at the onset of the illness; later lost to follow up due to a trip to a neighbouring state for the burial of his grandmother who died from a febrile illness and bleeding dyscrasias. With the persistence of symptoms, repeat MP at the same hospital revealed ++. He was subsequently referred to our facility due to the ongoing Strike action. He had right inguinal herniorrhaphy at age 3 years and had no history of blood transfusion. He was not a known sickle cell disease, asthma or seizure disorder patient. He was prescribed antimalarials, antibiotics, analgesics, and haematenics from the referring hospital. He had ingested traditional medication in the course of present illness. He had no known drug allergies.

KH's mother booked her pregnancy at the gestational age of three months at the same teaching hospital. She took routine antenatal medications as prescribed. There was no history of febrile illness during the pregnancy, delivery was uneventful, he weighed 2.8Kg, and had uneventful neonatal period. He achieved neck control at three months, sat without support at five months, crawled at eight months and walked without support at eleven months. He had OPV_0, BCG and HBV_0 one week after birth; at six weeks, he was given OPV_1, DPT_1 and HBV_1; at ten weeks, he got OPV_2, DPT_2; at fourteen weeks he got OPV_3, DPT_3 and HBV_2; and got Measles, Vitamin A and Yellow fever vaccines at nine months. KH was not breastfed because his mother had HIV and chose not to breasted. He was given breast milk substitute for three months and then introduced to pap, and regular family diet from five months of age.

He was the second of four children in a monogamous setting. He was a JS1 student. They lived in a 2-bedroom house with water cistern toilet facility, and underground well as their source of water. His mother was a secondary leaver and housewife. His father worked with a Federal government parastatal. Neither of them took alcohol nor tobacco. KH's illness started two days after the death of his grandmother; who had a febrile illness with diarrhoea, and was brought from the village in Benue state to be treated in Jos. Two days before her death, she started passing blood per rectum. His younger sister has similar complaints, although with jaundice in addition. His healthcare financing was from the National Health Insurance Scheme (NHIS).

Table 1: Examination findings

Date	Respiratory Rate	Temperature	Pulse Rate	Weight
Admission	28 cycles per minute	39^{O}C	124 beats per minute	25Kg
Days 3	32 cycles per minute	38.4^{O}C	94 beats per minute	24Kg
Day 6	28 cycles per minute	37^{O}C	140 beats per minute	24Kg
Day 9	20 cycles per minute	36.3^{O}C	130 beats per minute	24Kg
Day 12	20 cycles per minute	36.5^{O}C	100 beats per minute	24Kg
Follow up I	22 cycles per minute	36.6^{O}C	102 beats per minute	24Kg
Follow up II	20 cycles per minute	36.7^{O}	108 beats per minute	25Kg

Physical Examination

He was an adolescent, ill looking, conscious, dehydrated, pale, anicteric, febrile (39.0^{O}C), no palpable lymphadenopathy or pedal oedema. His RR was 28cpm, his breath sounds were vesicular, and his oxygen saturation was 90% on room air. His PR was 124bpm and small volume. He had first and second heart sounds only. He was lethargic, conscious with of GCS 15/15, had no signs of meningeal irritation or neurologic deficits. He had right upper quadrant and epigastric tenderness, others were normal. His weight was 25Kg.

Table 2: Laboratory Workup

Parameter	Result	Reference Range
Blood urea nitrogen (BUN)	2.4	Male: 3.2 – 7.1 mmol/L Female: 2.5 – 6.1 mmol/L
Creatinine	29	Male: 55 – 110 µmol/L Female: 46 – 92 µmol/L
Full blood count (FBC)	TWCC 11,800; N79, L18, M2, E1, HCT 13%, 37%**	WBC: 4.0 – 10, 000/mm^3 N: 50 – 80%, L: 25 – 50%, M: 2 – 10%, E: 0 – 5%, Basophil: 0 – 2%
Retroviral screening (RVS)	Non-reactive	Non-reactive
Malaria parasite (MP)	+, Not seen*, Not seen**	No MP seen
Urinalysis	Protein++, Blood+, Leucocyte+, Pus cells+, RBC++	Negative: Protein, Blood, Nitrite, Leucocytes, RBCs
Electrolytes	Na 149 K 5.4 Cl 115	Na: 137 – 145 K: 3.6 – 5.0 Cl: 98 – 107
Transaminases	AST 315, 76* ALT 126, 41*	AST: Male; 14 – 50 U/L Female; 8 – 39 U/L ALT: Male; 13 – 61 U/L Female: 3 – 42 U/L

***At the end of treatment** ****At Follow up visit**

Results of Investigations

Malarial Parasite (MP), Full Blood Count (FBC) were analyzed; Urea, Creatinine, Electrolytes (E/U/C) and Transaminases were investigated to rule out functional limitations of the renal and hepatic systems, respectively; Urinalysis (UA) and Retroviral Screening (RVS) were checked. The Laboratory results were as follows: the RVS was non-reactive; Aspartate transaminase (AST) was elevated 315 (14-50), Alanine transaminase (ALT) was elevated 126 (13-61); Full blood count (FBC) was elevated 11, 800, N79, L18, M2, E1, Packed cell volume (PCV) was reduced 13 (40-54%); Urinalysis showed Protein ++, Blood +, Leucocyte +, pus cells +, RBC +; and Malaria parasite (MP) + was seen.

PCR Result

Blood sample was sent to the Virology Unit/Central Research Laboratory, LUTH, Lagos; this showed positive results for Lassa fever and Yellow fever.

Diagnosis

The overall clinical presentation as initially suspected was consistent with diagnosis of Viral haemorrhagic fever (VHF): Yellow fever and Lassa fever.

Interventions and Outcome

KH was admitted into the Isolation Unit of the Hospital. Universal precautions/barrier nursing was instituted. Available evidence indicate that most nosocomial VHF cases have been acquired by inoculation with virus contaminated instruments or by direct contact with blood or other body fluids from infected patients.[4] Patients with Yellow fever should be nursed in mosquito-protected premises. Non-immune Yellow fever contacts should be immunized without delay. Preventive measures should apply to doctors, nurses, and anyone else (such as visitors, technicians, clerks, cleaners, messengers, and laboratory personnel) who may encounter a patient infected with VHF or with potentially infectious blood or body fluids.[4]

The following investigations were requested; LFTs, RVS, urinalysis, FBC, and MP. Antivirals (Ribavirin), Antipyretics (Acetaminophen), Intravenous fluids (Dextrose saline), Artesunate/artemether-lumefantrine, blood transfusion, Frusemide (pre and post transfusion), and Antibiotics (Ceftriaxone) [before the release of PCR result] were used at different times in the course of his twelve days on admission. Prognosis was discussed with parents and relatives.

Hospital Personnel and logistics were mobilized for his care. Representatives of the Epidemiology Unit of the state ministry of health were also on ground to provide support (contact tracing and testing blood samples of suspected cases) and logistics (personal protective equipment[PPE] – Goggles, Gloves, Gowns, Aprons, Boots; Chlorine water; Bin liners; and Hand sanitizers).

DISCUSSION

The clinical presentation by KH could have been Malaria (which was still positive after several treatments, retreated with Artesunate/Artemether-lumefantrine), Enteric fever, or other VHFs (Marburg, Ebola, Dengue, Crimean-Congo Rift valley, etc.).[5] The diagnosis of Yellow fever – Lassa fever co-infection was coincidental, although was suspected by the managing team due to the patient's non-response to the usual antimalarial and antibiotics for common causes of fever in our environment. This necessitated the request for their testing and subsequent confirmation.

Yellow fever virus (*Flavivirus*) and Lassa fever virus (*Arenavirus*) are both RNA viruses that lead to illnesses with similar clinical symptoms, with slight

difference in clinical management – supportive care only in Yellow fever, although both supportive and use of antivirals (Ribavirin) in Lassa fever management.[6,7] Yellow fever unlike Lassa fever has a vaccine that is protective for ten years (booster doses not needed).[8,9] KH had Yellow fever vaccination (charted on his Immunization card) at nine months of age, although he still succumbed to the same illness nine years later.

The essence of reporting this Yellow fever – Lassa fever co-infection is to show that high indices of suspicion and prompt attention, when provided can improve outcomes for these VHFs. PCR testing for VHFs though not readily available in Jos, can be carried out in other Reference Laboratories within Nigeria (LUTH Lagos state, ISTH Edo state, FETHA Ebonyi and Gaduwa Abuja).

CONCLUSIONS AND RECOMMENDATIONS

Viral haemorrhagic fevers such as Yellow fever and Lassa fever (co-infection), although rare, pose a serious challenge to the lives of patients and their relatives. This is more so in low- and medium-income countries where skilled personnel to manage such complicated cases is grossly lacking. Managing teams should endeavour to have high indices of suspension when faced with atypical presentations or nonresponse to routine treatment for common illnesses. Concerted efforts must be made by healthcare workers to acquire the necessary competencies to manage such cases. Resources such as Clinical Workshop on Diagnosis and Case Management of VHFs by Irrua Specialist Teaching Hospital and Nigeria Centre for disease Control, will prove beneficial in this regard.

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CONFLICT OF INTEREST

We declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

REFERENCES

1. WHO. Detection and investigation of serious events following yellow fever vaccination, Geneva, World Health Organization (WHO); 2008.
2. Clinical Management of Lassa fever. Standard Operating Procedures for Lassa Fever Case Management. Nigeria Centre for Disease Control, Abuja (NCDC). 2017[cited 2018 Dec 17]; Available from: http://www.ncdc.gov.ng
3. WHO. Lassa fever - Fact Sheet, 2017 [cited 2017 Jul 18]. Available from: http://www.who.int/mediacentre/factsheets/fs179/en/
4. Ericson CD, Steffen R, Isaacson M. Viral Haemorrhagic Fever Hazards for Travelers in Africa. Clinical Infectious Diseases. 2001(33); 10:1707-12.
5. Viral haemorrhagic fevers. CDC 2014 [cited 2019 Jan 19]. Available from: http://www.cdc.gov/vhf/index.htm
6. WHO. Yellow fever Fact sheet 2013 [cited 2018 May 13]. Available from: http://www.who.int/mediacentre/factsheets/fs100/en/
7. WHO. "Lassa fever" Fact Sheet 2016 [cited 2018 Mar 27]. Available from: http://www.who.int/mediacentre/factsheets/fs179/en/

8. Yun N.E, Walker D.H. Pathogenesis of Lassa fever. Viruses 2012;4(12): 2031-48.
9. WHO. Yellow fever vaccination booster not needed. News release [Internet] 2013; cited 2018 Mar 28]; Available from http://www.who.int/mediacentre/news/releases/2013/yellow_fever_20130517/en/