Case Report

Successful management of Lassa fever disease in a Nigerian with haemoglobin SC disease at the Lassa fever management centre of Alex Ekwueme Federal University Teaching Hospital Abakaliki, Nigeria

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Abstract

Background: Sickle cell disease (SCD) is a group of inherited blood disorders resulting from the presence of mutated form of haemoglobin, known as haemoglobin S (HbS). Inheritance of abnormal HbS can occur in homozygous form (HbSS), called sickle cell anaemia or in combination with other haemoglobin variant such as HbSC. There is paucity of study on the management of Lassa fever disease in patients with sickle cell disease. The objective of this study is to report a successfully managed case of Lassa fever disease in an adult with sickle cell disease (HbSC).

Case presentation: We report a 25year old man living with sickle cell disease (HbSC), who presented to the Alex Ekwueme Federal University Teaching Hospital Abakaliki, with complaint of fever, malaise, weakness of 6 days and abdominal pain, passage of watery stool, nausea, vomiting and generalised joint pain 2 days prior to presentation. Following physical examination, a provisional diagnosed of vaso-occlusive crisis with gastroenteritis with background malaria was made. Worsening of symptoms despite treatment with antimalarial, antibiotics and analgesics, led to the suspicion of Lassa fever which was confirmed with polymerase chain reaction (PCR). Patient was then treated with ribavirin, recovered completely with no residual complication and was subsequently discharged.

Conclusion: This case illustrates the importance of having high index of suspicion following persistent fever with non-response to treatment. Death due to Lassa fever disease can be prevented by early presentation to the hospital, high index of suspicion and close monitoring, avoiding delays to commencement of treatment.

Key words: Case report, Haemoglobin SC, Lassa fever disease, sickle cell disease, Nigeria.

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Introduction

Sickle cell disease (SCD) is a group of inherited blood disorders resulting from the presence of mutated form of haemoglobin, known as haemoglobin S (HbS).[1] Inheritance of abnormal HbS can occur in homozygous form (HbSS), called sickle cell anaemia or in combination with other haemoglobin variant such as HbSC. Sickle cell anaemia is the most common form of SCD found in Nigeria.[2] Haemoglobin S results from mutation in the β-globin gene with consequent replacement of glutamic acid with valine at position 6 of β-globin chain. The effect of this mutation is that haemoglobin will crystalize and form long fibres called tactoids under hypoxic condition with distortion of the shape of red blood cell from discoid to sickle or C-shape.[1] The sickle shapes cells are less flexible and cannot easily pass through microvasculature with vaso-occlusion and resultant pain which can affect any part of the body. Moreover, the abnormally shaped cells are prematurely haemolysed with resultant anaemia, in addition to other complications. There is a great variation in clinical manifestation of patients with SCD with the degree of anaemia, frequency of crisis and the organ systems involved vary markedly from person to person due to certain environmental and genetic factors.[3]

Lassa fever is an acute viral haemorrhagic illness that occurs in West Africa and caused by the Lassa virus belonging to Arenaviridae.[4] It is a zoonotic disease that is transmitted to humans via contact with food or household items contaminated with faeces or urine of infected multimammate rat called *Mastomys natalensis*. Human-to-human infections can occur through direct contact with the urine, faeces, blood or other body fluids of an infected person. Human-to-human transmission occurs in both community and health-care facilities with inadequate infection prevention and control measures.[5] Possibility of sexual transmission has also been reported.[6] Lassa fever disease affects all age groups and both sexes. Many people (about 80%) infected with Lassa fever usually have mild symptoms and are undiagnosed, with only about 20% manifesting with clinical illness.[4,7]

The clinical manifestation of Lassa fever disease is so diverse and non-specific, hence can mimic other viral haemorrhagic fevers such as Ebola virus disease or other diseases that causes fever such as malaria, with consequent difficulty and delay in making diagnosis.[8] High index of suspicion in diagnosis and early treatment is key in improving outcome. The incubation period of Lassa fever ranges from 2 to 21days.[9] When symptomatic, the onset of the disease is gradual manifesting with fever, malaise, and weakness. Few days following the initial symptoms, other symptoms may follow, such as headache, muscle pain, chest pain, sore throat, nausea, vomiting, abdominal pain, diarrhoea, and cough.[9] In severe cases facial oedema and bleeding from the mouth, nose, gastrointestinal tract, vagina, or other orifices may develop. In later stages of Lassa fever disease, shock, tremor, seizures, disorientation, and coma may occur. Deafness occurs in 25% of patients who survive the disease and hearing returns partially after 1–3 months in about half of these cases.[10] In fatal cases, death usually occurs within 14 days of onset of the disease without treatment, due to multi-organ failure.

Sickle cell disease is a genetic disorder while Lassa fever disease is an infectious disease. The management of each of these conditions is mainly supportive. However, Ribavirin has been shown to significantly reduce mortality associated with Lassa fever disease especially if treatment is commenced early in the course of the disease.[11] There is paucity of study on the management of Lassa fever disease in patients with sickle cell disease. The objective of this study is to report a successfully managed case of Lassa fever disease in an adult with sickle cell disease (HbSC).

Case Presentation

Mr GK is a 25year man living with sickle cell disease (HbSC) who presented to our facility with complaint of fever, malaise, weakness of 6 days and abdominal pain, passage of watery stool, nausea, vomiting and generalised joint pain 2 days prior to presentation. Fever was high grade and intermittent with associated headache, chills and rigor, loss of appetite, generalised joint pain and passage of watery stool which was non mucoid nor blood stained. There was no associated cough, no urinary symptoms. No history of contact with anybody with cough or fever.

For the above complaints, patient visited a patent medicine dealer who gave him some medications including anti-malaria drugs but the symptoms persisted before he decided to present to our hospital for expert management.

Examination showed a young man in moderate painful distress, febrile to touch, mildly icteric, mildly pale, acyanosed, moderately dehydrated, with no pedal

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oedema and no peripheral lymphadenopathy. Patient was conscious and alert with no sign of meningeal irritation.

Temperature was 39.6^{0}C, pulse rate was 90 beats per minute, respiratory rate was 28 cycles per minute and blood pressure was 120/80mmHg. There was vesicular breath sound on auscultation of the chest, heart sound 1 and 2 was heard. There was no murmur. Abdomen was full and moves with respiration. There was generalised moderate tenderness. Liver and spleen were not enlarged and kidneys were not ballotable. Bowel sound was present and normoactive. Examination of the musculoskeletal system showed mild tenderness at both knee and ankle joints. Other systems showed no abnormality. A provisional diagnosed of vaso-occlusive crisis with gastroenteritis on a background of malaria was made.

Investigations done reported malaria parasite – negative, packed cell volume (PCV) was 30%, white blood cell count was 15.1 x 10^9/l and platelet count was 361 x 10^9/l. Screening for hepatitis B, C, HIV were all negative. High performance liquid chromatography for haemoglobin (HB) phenotype reported HbA (0%), HbS (44.7%), HbC (41.5%), HbF (1.8%), HbA2 (1.7%), HbA1C (3.5%). Urinalysis showed protein and bilirubin. Blood culture was not done due to financial constraint. Patient was placed on intravenous infusion (dextrose saline 1liter 8hourly for 48hours), anti-malaria drug (intramuscular Emal 150mg daily for 3days) which was already commenced based on clinical suspicion before the result of malaria parasite test was available. Patient also received analgesic (intramuscular pentazocine 30mg 6hourly and intramuscular paracetamol 600mg 8hourly, both for 48hours then changed to tablet DF118 30mg 8hrly for 5days and paracetamol 1gram 8hrly for 3days). In addition, antibiotics (intravenous ciprofloxacin 200mg 12hourly and metronidazole 500mg 8hourly, both for 5 days) and haematinics (folic acid, multivitamin, pyridoxine, vitamin B complex, vitamin C) were also given.

Despite the treatment, patient was not getting better, fever persisted with extreme weakness and patient developed sore throat with pain on swallowing. Two days after development of sore throat, peripheral lymphadenopathy involving the cervical, axillary and inguinal lymph nodes with the largest measuring 3 by 4cm, non-tender, mobile and film in consistency, was noted. At this point, Lassa fever disease was suspected, being endemic in Abakaliki, for which investigation was done and PCR result of Lassa fever disease was positive. Patient was then isolated from the general ward and admitted in "Lassa Ward" located in our facility where Lassa fever and other viral haemorrhagic fevers are managed. Then treatment for Lassa fever was commenced with ribavirin for 10 days. While on treatment with ribavirin, patient's PCV initially dropped to 20% but started rising again when ribavirin was completed. The drop in PCV level was managed with haematinics (including Tablet multivitamin 1 8hourly, B-complex 1 8hourly, folic acid 5mg daily, vitamin C 100mg 8hrly, pyridoxine 50mg 12hourly – all for 3weeks), without blood transfusion. Patient started getting better, fever started subsiding, sore throat and pain on swallowing started reducing. All other symptoms improved and patient gradually recovered fully with no residual complication, though lymphadenopathy resolved gradually over about five weeks. Repeated Lassa PCR done three weeks after was negative and he was subsequently discharged home after being on admission for three weeks.

Discussion

This report showed that sickle haemoglobin may not be protective against Lassa fever disease unlike malaria where sickle haemoglobin was reported to be protective, especially for sickle cell trait with co-inheritance of sickle and normal haemoglobin.[12] In the index case, there is co-inheritance of two abnormal haemoglobin variant, haemoglobin S and C, with absence of normal adult haemoglobin and that may have contributed to the clinical manifestation of severe disease in this case.

The index patient presented with non-specific symptoms including fever, malaise, weakness for which he tried to treat himself at home by getting over-the-counter anti-malaria medication but his condition persisted before he decided to seek expert care in our centre. Mortality resulting from Lassa fever disease is usually due to organ damage and failure due to delay in diagnosis and treatment.[11] This is due to the fact that Lassa fever usually present with non-specific symptoms and can easily be confused with other diseases that causes fever and similar symptoms such as malaria, typhoid fever and other viral haemorrhagic fevers. Therefore, high index of suspicion is required to enhance prompt diagnosis and treatment in order to reduce mortality associated with Lassa fever disease.

Good response of the patient to ribavirin administration still supports the fact that ribavirin is the drug of choice

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for the treatment of Lassa fever disease.[11] It is a guanosine analogue which has broad-spectrum activity against many DNA and RNA viruses, including Lassa virus.

It has been reported that about 10% of patients treated with ribavirin will develop severe anaemia and may require dose reduction, which may compromise sustained virologic response.[13] The index patient developed severe anaemia with reduction in PCV from 30% to 20% following treatment with ribavirin. However, there was improvement in anaemia on completion/ stoppage of ribavirin, in addition to administration of haematinics (including Tablet multivitamin 1 8 hourly, B-complex 1 8hourly, folic acid 5mg daily, vitamin C 100mg 8hrly, pyridoxine 50mg 12hourly – all for 3weeks), without the need for blood transfusion. Ribavirin has been reported to cause haemolytic anaemia which is related to ribavirin accumulation within erythrocytes.[14] This will result to inhibition of intracellular energy metabolism and oxidative damage to erythrocyte membranes, with consequent extravascular haemolysis by the reticulo-endothelial system. Haemolysis is known to be part of the disease course in sickle cell disease and contribution of ribavirin induced anaemia to the haemolysis worsened the anaemia with rapid decline in PCV. Impairment in renal function may also contribute to ribavirin-induced anaemia but there was no evidence of impaired renal function in our patient throughout the course of treatment. Haemorrhage is a well-known clinical manifestation of Lassa fever disease especially at the terminal stage,[11] but the index patient did not manifest with any bleeding diathesis throughout the course of the illness till recovery. Developing haemorrhage in addition to the already existing haemolysis would have worsened the anaemia even further with possible blood transfusion requirement. Haemoglobin S has been reported to release oxygen easily to the tissues compared to haemoglobin A,[15] and that may have contributed to the patient being haemodynamically stable at the PCV of 20% without symptoms that may warrant blood transfusion.

Good health seeking behaviour exhibited by the patient also contributed to this success story. His decision to present himself for expert care with failure of home treatment is an action that should be emulated. Death following Lassa fever disease is usually due to delays in presenting to the hospital, since fatality usually occur within 14 days of onset of the disease without treatment.[16]

Conclusion

This case illustrates the importance of having high index of suspicion following persistent fever with non-response to anti-malaria and antibiotics. Death due to Lassa fever disease can be prevented by early presentation to the hospital, high index of suspicion and close monitoring, avoiding delays to commencement of treatment.

Declarations

Consent: Patient's consent was sort and obtained before writing this case report. Patient perceive the diagnosis and treatment as an uncommon occurrence which should be shared with others so that anybody with similar occurrence subsequently can be better managed to reduce associated complications and mortality.

Conflict of interest: The authors declare no conflict of interest**.**

Authors' contribution: UNI, UGC, CNM, ACO, EEO, NEI were involved in the management of the patient and conceived the idea of sharing the success story with the research community. UNI, UGC, ACO, UCN wrote the manuscript. ANA, CNM and EEO revised the manuscript. All the authors approved of the manuscript.

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