Acute abdominal pain in patients with lassa fever: Radiological assessment and diagnostic challenges

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ABSTRACT

Background: To highlight the problems of diagnosis and management of acute abdomen in patients with lassa fever. And to also highlight the need for high index of suspicion of lassa fever in patients presenting with acute abdominal pain in order to avoid surgical intervention with unfavourable prognosis and nosocomial transmission of infections, especially in Lassa fever-endemic regions.

Materials and Methods: A review of experiences of the authors in the management of lassa fever over a 4-year period (2004-2008). Literature on lassa fever, available in the internet and other local sources, was studied in November 2010 and reviewed. Results: Normal plain chest radiographic picture can change rapidly due to pulmonary oedema, pulmonary haemorrhage and acute respiratory distress syndrome. Plain abdominal radiograph may show dilated bowels with signs of paralytic ileus or dynamic intestinal obstruction due to bowel wall haemorrhage or inflamed and enlarged Peyer’s patches. Ultrasound may show free intra-peritoneal fluid due to peritonitis and intra-peritoneal haemorrhage. Bleeding into the gall bladder wall may erroneously suggest infective cholecystitis. Pericardial effusion with or without pericarditis causing abdominal pain may be seen using echocardiography. High index of suspicion, antibody testing for lassa fever and viral isolation in a reference laboratory are critical for accurate diagnosis. Conclusion: Patients from lassa fever-endemic regions may present with features that suggest acute abdomen. Radiological studies may show findings that suggest acute abdomen but these should be interpreted in the light of the general clinical condition of the patient. It is necessary to know that acute abdominal pain and vomiting in lassa fever-endemic areas could be caused by lassa fever, which is a medical condition. Surgical option should be undertaken with restraint as it increases the morbidity, may worsen the prognosis and increase the risk of nosocomial transmission.

Key words: Acute abdomen, diagnosis, lassa fever, radiology, ultrasound.

INTRODUCTION

Lassa fever is a type of viral haemorrhagic fever caused by lassa virus.¹² The disease is endemic in some countries of West Africa particularly Nigeria, Liberia, Guinea and Sierra Leone.¹³ About 300,000 to 500,000 infections are estimated to occur annually resulting in about 5,000 deaths in endemic regions.¹²⁴ The disease has also been carried sporadically through international travel from the endemic West African countries to Britain, Netherlands, United States, Japan, Germany, South African. Over 20 cases have been reported in developed countries and it is evident that only the countries with high reference laboratories have the capacity to conclusively identify the virus.¹²⁵⁶ Therefore, the other countries where it is not yet reported may not be necessarily free from the disease by export through international travel. Mastomys natalensis, a multi-mammate rat that is common and lives in bushes within and around people’s houses in endemic regions is the natural host of the virus.¹⁵ In homes in endemic regions, Mastomys natalensis constitute 50-60% of captured rats but only 5-20% of rats captured in and around farms; showing that the rats are more common within and around people’s houses.¹²⁷ Eating of food dried in the open floor, uncovered and contaminated with the saliva, urine and excreta of the rat is mostly responsible for the infection.¹² The prevalence of immunoglobin G (IgG) antibody detected in endemic areas is 12.3% of normal healthy people in Nigeria, 55% in Guinea and 52% in Sierra Leone.¹² The incubation period is 6-21 days and the disease affects all age groups and
both sexes.\textsuperscript{1,3} Infection at the extremes of life as well as in pregnant women carries worse prognosis.\textsuperscript{1,5}

The clinical features of the disease are similar to those of other infections that are common in endemic areas such as malaria, typhoid fever, cholecystitis, hepatitis, yellow fever, meningitis, gastroenteritis and other common febrile illnesses.\textsuperscript{1,3,6} The disease is symptomless in over 80% of the infected people but 20% may show severe systematic symptoms and signs.\textsuperscript{1,2,3} It is this 20% that constitute the hospital admitted cases. The disease is also very difficult to diagnose clinically.\textsuperscript{1,3} The presenting complaints include persistent fever of about 38°C which is unresponsive to antimalarial treatment and conventional antibiotics, rigors, pharyngitis (sore throat), retro-sternal chest pain, vomiting, abdominal pain, back pain, muscle pain, weakness, cough, shortness of breath, yellowness of eyes, puffy face/neck/jaw, lymphadenopathy, constipation, gastro-intestinal bleeding, rib pain and tenderness, restlessness, dizziness, confusion and coma.\textsuperscript{1,2}

Physical examination may show mucosal petechial bleeding from the mucosa of mouth, nose, vagina and anus. Pleural and pericardial effusion, ascites and scrotal fluid collection often occur and these imply signs of serositis. Other recorded findings are hyphaema, abdominal distension, lymphadenopathy, signs of intestinal obstruction, shock, multiple organ failure, coma and generalised oedema.\textsuperscript{1,3,5,8} Case fatality rate occurs in 1-2% in the general population of infected people in endemic regions while hospital mortality rate is 10-87%.\textsuperscript{2,3} ISTH, Irrua, Edo State, is the most active lassa fever treatment centre in Nigeria.

**MATERIALS AND METHODS**

This is a review article involving the experience of the authors in the management of lassa fever cases over a 4-year period (2004-2008) and publications on lassa fever. The available literature on the internet and other local sources including libraries, and hospital records were studied for up to 2010. Relevant articles were reviewed and the necessary information extracted. Practical experience of the authors in clinical management of lassa fever cases over a 4-year period (2004-2008) at Irrua Specialist Teaching Hospital (ISTH), formed the backbone of the study. ISTH is a Centre of Excellence for the treatment of lassa fever in Nigeria. Important areas of sources of errors that could lead to false positive or false negative diagnosis of lassa fever and possible sources of complications were also reviewed.

Many cases had radiological assessment to exclude other diseases. A few cases with radiological investigation that had clinical diagnosis using criteria provided by the Centre for Disease Control and Prevention/World Health Organisation (CDC/WHO) and the Federal Ministry of Health (FMoH) of Nigeria, Abuja are presented in this study. Laboratory studies were also used to arrive at the diagnosis and in most cases, both the clinical diagnostic criteria and the supporting laboratory studies were used for the diagnosis.\textsuperscript{1,2,8,11,12} The criteria for clinical diagnosis include: 8,10

Major criteria are:
(i) Abnormal bleeding from mouth, gum, nose, vagina, urinary tract; (ii) Haemoptysis, bleeding from the ear; (iii) Swollen neck and face; (iv) Red eyes or conjunctivitis (often bilateral); (v) Spontaneous abortion; (vi) Deafness during illness; (vii) Shock or systolic blood pressure <100 mmHg.

Minor criteria are:
(i) Sore throat; (ii) Headache; (iii) Diarrhoea; (iv) Leucopaenia; (v) Nausea and vomiting; (vi) Abdominal pain; (vii) Cough; (viii) Pleural effusion or ascites; (ix) Swollen lymph nodes, (x) Weakness; (xi) Proteinuria.

A combination of minor and major criteria is used to clinically diagnose lassa fever as follows.

**Possible lassa fever**
Persistently fever with two or more minor criteria and known contact with lassa fever cases.

**Probable lassa fever**
Persistently fever with any of the major criteria.

**Suspected case**
Patients with persistent fever (100°F or ≥37.8°C) not responding to antimalarial drugs or antibiotics.

**RESULT**

In the pathology of lassa fever, thrombocytopenia occurs early and may lead to spontaneous haemorrhage within the bowel wall with symptoms of pain, bowel distension and vomiting.\textsuperscript{1,6} Humoral inflammatory mechanisms causing partial bowel paralysis and subsequent dilatation have been implicated in some cases of bowel dilatation with diagnosis of intestinal obstruction.\textsuperscript{1,2,13} Enlarged, inflamed Peyer’s patches and lymph nodes also cause small bowels to dilate due to accumulation of gas and gastrointestinal contents proximal to the inflamed and tender aperistaltic areas.\textsuperscript{13} The bowel may be partially adherent to the inflamed glands leading to pain and further distension of the bowels.

Also, bleeding within the bowel wall causes ileus at the point of bleed, and contributes to subsequent dilatation of the bowel proximal to this point. Both, small and large intestines may be involved.\textsuperscript{12,14}

Contributions of one or all of the above listed mechanism may worsen the bowel dilatation, thus presenting with a
clinical and radiological features (diagnosis) of intestinal obstruction or acute abdomen.\textsuperscript{1,2}

Haemorrhage within the solid organs contained in the abdomen and pelvis, with the accompanying release of some enzymes which may contribute to tissue necrosis and pain.\textsuperscript{12,14} Bleeding into the wall of the gall bladder may erroneously lead to diagnosis of cholecystitis when symptoms such as right hypochondrial pains and tenderness on examination of right hypochondrium are felt by the patients in such cases.

Panorganotropism in lassa fever is observed as the lassa virus affects virtually all the organs of the body where it causes various types of abnormalities including organomegaly, inflammation with reactive fluid formation, and tissue necrosis. These may cause abdominal pain and distension.\textsuperscript{2,12,16} Bleeding within the omentum and the peritoneal sac also causes significant abdominal pain with minimal distension.

Significant amount of fluid may be seen within the uterus and the vagina on sonography studies even before the patients complains of vaginal bleeding. It should not be used as one of the criteria to diagnose ectopic pregnancy or mistaken for incomplete abortion as vaginal bleeding may occur in lassa fever. Pregnancy test will prove very useful. Therefore, in an endemic region if lassa fever is suspected, it is prudent to exclude it with ancillary investigation that could point or exclude the differential diagnosis.

It must be emphasised, however that, the most important factor in the diagnosis of lassa fever using clinical diagnostic criteria is high index of suspicion of the disease. Any patient with high fever that is unresponsive to antimalarial and conventional antibiotic treatments or fever of unknown origin, coming from any of the countries of West Africa that the disease is endemic should be suspected of the disease, assessed according to the earlier specified criteria following which laboratory tests should be conducted.\textsuperscript{1-5,17} Even the practice of sending samples for laboratory diagnosis of lassa fever in endemic areas also requires high index of suspicion since the clinical features of lassa fever are similar to other common febrile illnesses. Radiology studies done in those patients that later proved to be lassa fever are often very informative.

**RADIOLOGICAL ASSESSMENT**

Chest radiography may be normal at early stages and this may reassure the clinicians of the absence of chest pathology. This is deceptive as pulmonary haemorrhage, pulmonary oedema, and acute respiratory distress syndrome [Figure 1], may develop rapidly within hours or days.\textsuperscript{18,19} Aspiration pneumonia may also occur and may quickly lead to death.\textsuperscript{9}

Plain abdominal radiographs often show dilated gas-filled bowels of mild to moderate severity with no specific feature. This often leads to the diagnosis of intestinal obstruction or incomplete obstruction. Multiple air-fluid levels more than three in number and greater than 2.5 cm in diameter may be seen and may lead to diagnosis of dynamic intestinal obstruction. Occasionally large-diameter fluid-level may be observed due to dilated large bowels. Features of bowel haemorrhage appearing like thumb-printing may be seen especially in the transverse colon but this is more obvious on barium meal and enema examination which are currently not routinely indicated for patients with acute abdomen. Inflammation and enlargement of the Peyer’s patches may cause dilatation of the small intestines and may give the appearance of low small intestinal obstruction. This eventually leads to a serious confusion with typhoid enteritis or typhoid perforation.\textsuperscript{16-18}

Abdominal ultrasound often shows mild free intraperitoneal fluid collection. This should not be interpreted as ruptured viscus as it may alert the surgeon for surgical intervention which increases the morbidity, nosocomial transmission and may worsen the prognosis.\textsuperscript{1,2} It has been observed that free intraperitoneal fluid is not uncommon in patients with lassa fever.\textsuperscript{17} Occasionally, mild ascitic fluid may be localised in the pelvis, right iliac fossa or the sub-hepatic space due to dependency of these areas according to posture in lying down. This should not always be interpreted as acute appendicitis or ectopic pregnancy. The possibility of mild free intraperitoneal fluid which could be reactive ascites or haemoperitoneum in lassa fever should be remembered if high index of suspicion is applied. The bowels may show thickened wall with non-propulsive peristaltic activity on sonography. If bleeding occurs into the bowel wall, the bowel could be dilated and may be filled with fluid, allowing for their identification.
with ultrasound [Figure 2]. Lymphadenopathy may be seen in the abdomen and the presentation of major or minor criteria of lassa fever should raise suspicion of the infection.12,13,16-18

The kidneys may be enlarged due to oedema from bleeding and the calyces may show echogenic appearance from numerous small blood clots. With progression of the disease the kidney may be echogenic with reduction or loss of the cortico-medullary pattern [Figure 3]. Whether this is bleeding within the renal substance or other inflammatory changes, remain to be accurately ascertained but the renal changes are of different types and apart from the fact that the renal size is normal could suggest some other acute conditions. However, frequently the initial renal status may not be known in which the differential diagnosis becomes more difficult or uncertain. Electrolyte imbalance from kidney derangement soon sets in. This contributes to the bowel dilatation as a result of hypokalaemia which is also worsened by diarrhoea and vomiting that often accompany other clinical signs of the disease.17,18

Hypoechoic changes in the liver due to non-specific liver inflammation are frequently observed on sonography as well as mildly enlarged liver due to inflammation. These inflammatory changes are one of the causes of jaundice. Bleeding into the wall of the gall bladder may cause it to be thickened [Figure 4]. This could be confused with cholecystitis and blood clot within the gall bladder could be confused with cholelithiasis.12,16,17,19

Whenever any radiologist is carrying out abdominal ultrasound it is a good practice to study the heart. Useful signs that can be obtained from cardiac ultrasound include pericardial effusion, hypokinesia, dyskinesis (abnormal heart motion), intramural echogenic thrombus, cardiac tumours, echogenic pericardium due to inflammation and abnormal dilatation of one or more of the cardiac chambers. The most common lesion seen in the heart in patients with lassa fever is pericardial effusion.16,18 The need to assess the heart with echocardiography is also because some chest conditions like myocardial infarction can simulate acute abdominal pain.2,3,16

Soft tissue ultrasound of the eyes, submandibular glands and the scrotum/testes are invaluable in the study of patients with lassa fever using high resolution (7.5-15 MHz) ultrasound transducer. The eyes may show hyphaema due to bleeding within the anterior chamber. Bleeding into the scrotal sac may be seen as hydrocoele. It may be possible to identify bleeding within the scrotal muscle forming localised mild pseudotumour.2,3,16,17

Computed tomography (CT) of the brain or abdomen is not usually done as workup for acute abdomen in West Africa where lassa fever is endemic due to cost and the fact that the facility is not readily available in many centres. However, because patients with lassa fever can present with headache, drowsiness and coma, brain CT scans have been done in a number of cases.17,19 The lesions in the
brain are in the form of encephalitis or encephalomyelitis with periventricular and perigyrular hyperdense areas. Cerebral oedema may develop with effacement of the lateral ventricles. Without serological test for lassa fever, it is difficult to ascribe these to lassa fever even in endemic region because cerebral malaria and other common viral infections can produce similar features. CT scan of the abdomen in patient with lassa fever can show evidence of ascites, or haemoperitoneum, enlarged para-aortic lymph nodes, thickened bowel walls due to oedema, bowel-wall haemorrhage and inflammation. CT can exclude intra-abdominal mass lesion and many other causes of acute abdominal pain. Typhoid enteritis and vascular events may be wrongly diagnosed as the cause of the abdominal lesions.\textsuperscript{17}

Magnetic resonance is not readily available and its high cost greatly limits its use in sub-Saharan West Africa where lassa fever is endemic particularly in the rural areas. However, where it has been used to study the brain of a patient with lassa fever it shows multiple hyperintense periventricular lesions on T1-weighted images. The bowel wall distension and bowel wall thickening as demonstrated in CT will also be evident in abdominal MR imaging. Enlarged lymph nodes within the abdomen has also been observed.\textsuperscript{17}

**DIAGNOSTIC CHALLENGES**

The main challenge is that lassa fever is a medical and not a surgical condition, but it often presents with clinical features of acute abdomen which is in the domain of surgeons who lack the requisite diagnostic radiologic tools. It is therefore often contentious, whether the patient should go to the medical or surgical team or ward.

With high index of suspicion both the medical and surgical teams are expected to be able to clinically diagnose lassa fever in endemic regions. Samples can be sent to ISTH, Irrua for Polymerase chain reaction (PCR) testing within Nigeria, or to other reference hospitals/diagnostic centre in other countries. The result should be available within hours, no matter the State the hospital is situated in Nigeria. Protein urea, bleeding time and clotting time are important tests that should be done, since derangements are highly suggestive of lassa fever in symptomatic patients. However, once the clinical diagnosis of lassa fever have been made, it is a prudent practise to refrain from surgical intervention.\textsuperscript{2} Surgery is additional stress to a sick body and in the presence of lassa fever may worsen the outcome in patients.

Electrolyte and urea assessment are very vital. However, many of the radiological finding actually raise high suspicion of acute abdomen by other causes as lassa fever is not readily considered as a cause of acute abdomen in most endemic regions because of the problem of proving the diagnosis. Unless there is a discrepancy of co-existence of an independent acute abdominal condition and lassa fever, lassa fever should rest the surgical adventure. If this is not done the patient may succumb to some of the conditions discussed below.

Acute systemic disease with sepsis results in about 20\% of infected people with multiple organ failure due to primary systemic viraemia.\textsuperscript{1,2} Renal, hepatic, pulmonary and circulatory failure may occur at various degrees.\textsuperscript{1} This is one of the reasons while surgical option is reserved as the disease is a medical condition requiring supportive treatment in addition to treatment with ribavirin. The best result being obtained if treatment is started less than 6 days from the onset of the infection.\textsuperscript{1,2} At the autopsies of several patients that died from lassa fever, no particular lesion that could explain the death of the patients were found.\textsuperscript{13,18} In some other cases of such autopsies, however, various degrees of liver and splenic necrosis were found.\textsuperscript{13,17,18} These lesions are probably best treated medically.

In conclusion, high index of suspicion and applying recommended clinical diagnostic criteria are helpful in clinical diagnosis of lassa fever for those cases of lassa fever presenting with acute abdominal pain in lassa fever-endemic regions. Lassa fever is a medical condition and with high index of suspicion it is possible to diagnose lassa fever even in the presence of signs and symptoms of lassa fever that might suggest other surgical conditions. This is necessary in order not to worsen the prognosis and increases the risk of nosocomial transmission to the staff involved in surgical treatment.

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How to cite this article: Eze KC, Salami TA, Kpolugbo JU. Acute abdominal pain in patients with lassa fever: Radiological assessment and diagnostic challenges. Niger Med J 2014;55:195-200.

Source of Support: None declared. Conflict of Interest: None declared.

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