NIGERIAN INFECTIOUS DISEASES SOCIETY

Case Report

Yellow Fever and Hepatitis B Co-Infection in A Nigerian Girl with Acute Febrile Jaundice: A Case Report

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ABSTRACT

Yellow fever is a lethal re-emerging viral disease transmitted by infected Aedes mosquitoes. It is largely endemic in sub-Saharan Africa, with high risk of widespread outbreak in an unimmunized population. Recent outbreaks have been reported in several states in Nigeria. Yellow fever causes an acute febrile jaundice which can be confused with several endemic diseases, particularly viral hepatotropic infections such as hepatitis B, emphasizing the need for surveillance of co-viral pathogens during outbreaks. We report a rare case of yellow fever with hepatitis B co-infection in a 15-year-old girl who was successfully managed in a tertiary hospital in South-East Nigeria.

Key words: Yellow Fever, Hepatitis B, Co-infection, Nigeria, Surveillance.

INTRODUCTION

Yellow fever (YF) is a viral haemorrhagic disease transmitted by infected Aedes mosquitoes[1]. It is caused by YF virus, a reemerging virus that is endemic in several sub-Saharan African and South American countries. The World Health Organization (WHO) estimates that YF causes about 200,000 severe cases of disease with about 60 ,000 deaths globally every year despite the availability of an effective vaccine for over 70 years [2]. About 90% of the disease is said to occur in Africa with significant morbidity and mortality[3]. In 2017, YF re-emerged in Nigeria after 21 years of no case detection, with an outbreak in November 2020 that affected several states particularly Enugu, Delta and Bauchi[4]. As of 18 December 2020, Enugu state had reported 30 confirmed cases and 9 deaths with a case fatality rate of 1.5%[5]. The presentation ranges from sub - clinical illness that subsides within a few days to severe symptoms such as high fever, jaundice, abdominal pain, vomiting and bleeding from different body orifices[3].

The clinical presentation is divided into 3 stages: the period of infection, the period of remission, and, in about 15 % of cases, it progresses to the period of intoxication . No specific treatment exists for YF; however , supportive care if instituted early is critical to survival[3].

Hepatitis B is a potentially life-threatening liver disease that usually evolves into chronic hepatitis, liver cirrhosis and hepatocellular cancer resulting in significant morbidity and mortality[6]. The hepatitis B virus (HBV) is often transmitted through sexual intercourse, blood transfusion and during delivery. In Africa, hepatitis B is estimated to affect 60 million individuals, with at least 200,000 deaths per year[7].

Yellow fever causes acute febrile jaundice with similar presentation to other endemic diseases affecting the liver, particularly viral infections such as HBV[8]. Nigeria is endemic for both YF and hepatitis B due to a large non - immunized population and poor vaccination coverage, respectively.

To the best of our knowledge, there has been no reported cases of co-infection of YFV and HBV in the literature suggesting the need for active surveillance of these co-pathogens especially during YF outbreaks. Here, we report a rare case of YF and HBV co-infection in an adolescent girl who was successfully managed in a tertiary hospital in South - East Nigeria with supportive treatment.

CASE REPORT

A 15-year-old female secondary school student presented on referral to the isolation and treatment centre of the University of Nigeria Teaching Hospital (UNTH), Ituku / Ozalla, Enugu, Nigeria on the 11th of November, 2020 with a two-week history of high-grade fever associated with generalized throbbing headache, extreme fatigue, anorexia, nausea and vomiting; and three days history of vomiting of frank blood, passage of loose bloody stool, bloody urine and jaundice.

There was a history of outbreak of acute febrile illness in her locality and exposure to 10 confirmed cases of YF. She had received antimalarials and empirical antibiotics with poor response before referral. She reported receiving the YF vaccine at infancy according the National immunization guidelines. However, there was no past history of hepatitis B vaccination. On presentation, clinical signs comprised of temperature of 37.6 0C, pulse rate of 96/min, blood pressure of 100 /50 mmHg, respiratory rate of 28 cycles / minute and oxygen saturation was 91% on room air. She was pale, moderately jaundiced with tender hepatosplenomegaly.

Other systemic examination findings were unremarkable. An impression of YF to rule out fulminant hepatitis was made. Following notification to the Enugu State Ministry of Health (as part of the YF surveillance program), blood sample for YF virus RT-PCR was collected and sent to the National Reference Laboratory Abuja. The YF virus RT-PCR test returned positive. Her Hepatitis B surface antigen (HBsAg) test also turned out positive. She had markedly elevated transaminases. Other laboratory and ancillary results are shown in Table 1.

Table 1: Laboratory parameters of the patient

Parameters	Normal Ranges	Result (on Presentation)	Interpretation	Result (after 4 days)
Haemoglobin (g/dL)	11.5-13.5	9.0	Anaemia	
White blood cell (X 10^9/L)	4.5-13.5	3.5	Neutropenia	
Neutrophils %	40-75	55	Normal	
Lymphocytes %	20-45	45	Lymphocytosis	
Platelet (X 10^9/L)	100-400	51	Thrombocytopenia	
Peripheral Blood film		White cell appeared normal	Thrombocytopenia , platelet clumping	
Malarial Parasite		++		
Random blood glucose (mmol/L)	4.0-10	8.5	Normal	
HIV Screening		Seronegative	Normal	
Hepatitis B surface antigen		Seropositive	Abnormal	
Hepatitis C Antibody		Seronegative	Normal	
Urinalysis		++ blood, ++ Bilirubin	Haematuria, Bilirubinuria	
Total Bilirubin (umol/L)	8-17	409	Markedly elevated	412.4
Conjugated Bilirubin (umol/L)	<8.0	390.9	Markedly elevated	365.9
Alanine Transaminase (IU/L)	3-15	100	Markedly elevated	72
Aspartate Transaminase (IU/L)	5-18	114	Markedly elevated	96
Alkaline Phosphatase (IU/L)	25-92	81	Normal	79
Total Protein (g/L)	60-80	55	Hypoproteinemia	
Serum Albumin (g/L)	30-50	26	Hypoalbuminemia	
Serum Globulin (g/L)	18-30	29	Normal	
Sodium (mmol/L)	135-145	140	Normal	
Potassium (mmol/L)	3.5-5.0	2.4	Hypokalaemia	
Bicarbonate (mmol/L)	22-28	25	Normal	
Chloride (mmol/L)	97-108	102	Normal	
Urea (mmol/L)	2.1-7.1	4.3	Normal	
Creatinine (umol/L)	53-150	145	Normal	
Yellow Fever PCR		Positive		
Glomerular Filtration Rate (GFR) (mls/min/BSA)		51.3	Evidence of Renal Impairment (AKI)	

Complete panel of markers of HBV infection, viral load and an abdominal ultrasound scan were requested but she was unable to do the tests due to financial constraint. She was diagnosed with severe YF with HBV co-infection. The treatment regimen comprised intravenous (IV) ringer's lactate 500 mls 8-hourly to correct dehydration, 1g IV ceftriaxone daily for superimposed bacterial infection, 10mg IV metoclopramide daily to control the vomiting, 40mg IV omeprazole daily to prevent stress related gastric ulcers, one tablet of artemether-lumefantrine double strength twice for 3 days, and haematenics. Yellow fever vaccination of care giver and other close contacts was done. After one week on admission, she developed acute kidney injury (AKI) with bilateral leg swelling. Subsequently, with conservative management, she improved and was discharged after two weeks of hospitalization following remarkable improvement of her clinical symptoms and biochemical parameters with a plan to continue follow-up on outpatient basis. Unfortunately, she was lost to follow-up.

DISCUSSION

To the best of our knowledge, this is the first reported case of YFV and HBV co-infection in sub-Saharan Africa and probably in the world despite the endemicity of these viruses in our setting. The Nigerian Center for Disease Control (NCDC) reports that 80 % of YF cases were found in individuals who were 30 years old and below with an average age of 15 years[5]. This is consistent with the age of the index case.

The clinical presentation of fever, vomiting, abdominal pain, and jaundice in the case, supports the diagnosis of acute febrile jaundice, a clinical syndrome that can be due to parasitic infection (severe malaria), bacterial infection (leptospirosis) or viral infection (viral haemorrhagic fevers or viral hepatitis). Although the history of bleeding from different body orifices and acute kidney injury can occur in both YF and fulminant hepatitis, the diagnosis of YF was further strengthened by the history of epidemiological links with PCR-confirmed YF cases at the peak of a YF outbreak season.

There is no readily available information in the literature on the impact of co-infection of YF and hepatitis B on the severity and outcome of patients with acute febrile jaundice, however, some reports indicate that cases of viral hepatitis B co-infection with dengue fever, increases the chances of liver dysfunction, thereby increasing the severity of infection [9]. This has been attributed to aberrant cytokine secretion[10]. Argawal et al. found fulminant hepatitis in an HBV-dengue virus co-infected carrier in India supporting the argument that co-infection could potentially lead to worse liver disease severity[11]. This evidence, from a commoner arbovirus, supports the possibility that HBV co-infection with YF could be responsible for the severity observed in the index case.

This case also brings to the fore the challenges of diagnosis in settings of low resource where access to investigations is limited by out-of-pocket payment. The absence of test results for markers of hepatitis B chronic infection, viral load and abdominal ultrasound scan due to the patient's financial constraints is an acknowledged limitation of this report. This could have enabled us to better characterize the HBV component of her disease.

Despite the severe disease observed in the case, there was full recovery further buttressing the fact that good and early supportive treatment improves the chances of survival in severe YF. The age of our patient may have also contributed to her favourable outcome. It has been documented that persons at the extremes of life are more likely to have more severe YF illness and worse outcome[1].

Furthermore, the absence of history of hepatitis B vaccination and the possibility that the index patient had been due for yellow fever booster vaccination (considering that over 10 years had elapsed since her last dose) underscore huge gaps in vaccine uptake in our environment. This partly explains the relatively high burden of vaccine-preventable infections in Nigeria.

In conclusion, we report a rare case of YF and hepatitis B co-infection in a Nigerian girl with acute febrile jaundice. Active surveillance of epidemic prone diseases such as YF and mass YF vaccination during an outbreak season are effective ways to combat this re-emerging infectious disease. Public health authorities should sustain health education and vaccination campaigns for vaccine-preventable diseases.

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None.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical consideration

This case report was reviewed and approved by the Research and Ethics committee of the UNTH.

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