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Case report of multiple concomitant infections (HCV, HEV, Typhoid and Oral thrush) and their treatment challenges in a developing country

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Abstract

It is important to diagnose multiple infections timely, to avoid potential treatment complications. We report a case here with multiple infections, admitted to the ICU of a private healthcare facility, for ventilatory support. On admission, he had reactive hepatitis E and hepatitis C, was suspected of oral thrush, acute and chronic typhoid associated with headache, fever for one month, nausea for the last three days, yellow colored urine for seven days, and difficulty breathing. He was treated for four days, and afterward, removed from hospital care without the consent of the doctor in-charge while his condition was not stable. Several essential diagnostic tests were recommended but were not provided for by the caretakers. Unfortunately, the telephonic follow up brought the news of his sad demise a day after his discharge from the hospital. Poor financial conditions, lack of public funding, lack of awareness amongst caretakers, as well as the absence of trust in the national healthcare system, pose serious challenges for healthcare providers and lead to many such sad instances quite routinely in developing countries.

Introduction

Typhoid fever is a very common infectious disease in many countries [1]. It spreads through contaminated food or water and occasionally through direct contact with someone infected. It is often associated with several diseases as it starts with fever and is clinically indistinguishable from other diseases or infections [2]. Hepatitis C virus and Hepatitis E virus are major public health challenges in Pakistan [3]. HCV, a blood-borne virus, is mainly transmitted through syringes, sharing needles, or other drug-injection equipment and blood transfusion [4]. Hepatitis E virus is usually spread by the fecal-oral route. The most common source is fecally contaminated drinking water [5]. Here we report a young patient who was presented with fever, typhoid, HEV, and HCV infections. The purpose of this report is to describe the complications in diagnosis and treatment in a patient suffering from multiple infections and financial challenges in developing countries like Pakistan.

The Case

An 18-years old, 50 kg male with reactive HCV was admitted to the ICU for ventilatory support for labored breathing. On admission, he was found to have HEV, acute and chronic (long-term according to history presented) typhoid associated with a headache for 15 days, fever for 1 month, nausea for 3 days, and yellow color urine for seven days. Examination revealed a pulse rate of 86 beats/min, blood pressure of 120/80 mm Hg, respiratory rate of 18 breaths/min, and temperature of 98 °F. On auscultation, heart sound was not normal, air entry was a bit high and with sounds. Pupils and eyes were dry. The abdominal examination of the patient had normal results. The patient and his caretakers were altogether unaware or hesitant to answer any specific questions related to epidemiological risk factors as these diseases are still considered a social taboo.

To manage the breathing, VPAP was used. It was initiated with spontaneous/timed mode and later pressure increased to 20 cmH_2O inspiration and 5 cmH_20 expiration positive airway pressure with TiMax set at 3 sec. Investigations were conducted, lab reports showed hemoglobin 12.3 g/dL, lymphocyte count 0.51 x 10^ 9 eosinophil count 0.02, Red cell distribution with 15.8 %, urine chemical examination was 6.0 and erythrocyte sedimentation rate was (ESR) 17 mm/hr. Viral markers were positive for HEV. HCV was positive, later confirmed through HCV quantitative PCR. Typhoid was acute and chronic (**Table 1)**.

After two hours of admission to ICU, his temperature raised to 100 °F, pulse 98 bpm, and blood pressure 110/70 mm/Hg and after 24 hours B.P was 110/70 mm/Hg pulse 89 bpm and respiratory rate was still 18 breathe per min, his T.P.R chart (Temperature, Pressure, Respiratory rate) is given in **Table 2**. For emergency management, the medicines prescribed were Tab Paracetamol, Artemether-Lumefantrine 80/480 mg, Cefixime 400mg, 5% glucose, Mctoclopramid, Neubralfort morphe, Oxidil (Ceftiaxone sodium), Mepa-Merz-Granlaes, Esomax, Fluconazole, Omeprazole, Levofloxacil as different doses with different days (**Table 3**). Oral thrush was also diagnosed on 2nd day of admittance. He was maintained on 5% dextrose solution with no solid foods. There was further suspicion of malaria as well as tuberculosis during the brief hospital stay.

Table 1: Lab diagnostic tests and their Lab reports

Diagnostic tests	Lab Reports	Normal Values
Typhi dot	IgM + Acute IgG + Chronic	---
Anti HEV IgM	HAV IgM -ve HEV IgM +ve (11.42 <)	---
Hep Bs Ag	-ve	---
ESR	17 mm/hr	---
HCV Ab	reactive	---
Complete blood count (CBC)		
HGB	12.3 g/dL	13.5-18.0 g/dL
MCV	74L fL	80-100 fL
MCH	23.7L pg	27-33 pg
RDW	15.8 %	<16.4%
Lymphocytes	0.51 X 10^g/L	1.0-4.8 X 10^g/L
Eosinophil	0.02 X 10^g/L	0-0.5 X10^g/L

Table 2: TRP (Temperature, Pressure, Respiratory rate) Table. Daily reports of patient's blood pressure, pulse rate, temperature, and respiratory rate as recorded per day

Days	Time	Blood Pressure	Pulse	Temperature	Res
Admittance	07:00 p.m.	120/80	86/-	98 °F	18/-
	10:00 p.m.	110/70	98/-	100 °F	18/-
2nd	07:00 a.m.	110/70	89/-	A/F	18/-
	08:35 a.m.	110/70	86/-	A/F	18/-
	03:00 p.m.	110/70	84/-	98 °F	18/-
	05:45 p.m.	100/70	76/-	98 °F	18/-
	10:00 p.m.	100/70	80/-	98 °F	18/-
3rd	07:00 a.m.	110/70	82/-	98 °F	18/-
	08:30 a.m.	110/70	86/-	98 °F	18/-
	03:00 p.m.	90/60	84/-	98 °F	18/-
	06:00 p.m.	100/60	82/-	98 °F	18/-
	10:00 p.m.	100/60	82/-	98 °F	18/-
4th	07:00 a.m.	100/70	80/-	98 °F	18/-
	08:30 a.m.	100/60	72/-	98 °F	18/-
	01:00 p.m.	100/60	80/-	98 °F	18/-
5th	07:00 a.m.	90/60	82/-	98 F	18/-
	08:30 a.m.	100/60	88/-	98 F	18/-

Table 3: Drugs regimen followed during the hospital stay. Prescribed drugs, their dosage at different times, and the number of days of usage

Drug	Dosage	Usage duration	Usage days
Cefixime (200mg)	1 tab a day	3 days	Before admittance
Ceftiaxone sodium (500mg)	2 tab a day	4 days	Day 1 to day 4
Acetamenophen (500mg)	2 tabs thrice	2 days	After admittance
Esmeprazole (20mg)	1 tab	4 days	After admittance
L-Ornithin L-Aspartate Granules (5g)	2 tabs	2 days	After admittance
Cefixime (400mg)	1 tab 1 time a day	7 days	Discharge day
Artemether-Lumefantrine (80/480 mg)	1 tab 2 times a day	3 days	Discharge day
Acetamenophen (500mg)	2 tabs 2 times a day	3 days	Discharge day

The seemingly total failure of immune responses was an indication of some immunity-related disease, quite probable presence of Human Immunodeficiency Virus (HIV). Unfortunately, many of these questions remained unanswered due to lack of time as well as non-cooperation of the family with doctors and health care facility. Several specific laboratory tests were suggested but were negatively produced by the patient's caretakers.

Due to no visible improvement in the patient's condition and quite probable lack of financial support, the caretakers decided to get him discharged on the 5th day without the doctor's consent and took him home. Unfortunately, the telephonic follow-up brought the news of his sad demise as the next morning he passed away at his bed in his house without much needed medical attention.

Discussion

Direct invasion or immune-mediated endotoxemia are possible mechanisms of liver infection by *Salmonella typhi*. Severe infection of typhoid fever could be because by insufficient doses, reduced exposure to antibiotics, or a period of antimicrobial treatment. There are many cases of co-infection of *Salmonella parathyphi* with Hepatitis E in tropical areas and is quite common in endemic areas. Suspicion should be raised when the clinical presentation is atypical for any single pathogen [6]. Typhoid fever is a common infection in developing countries such as Pakistan. Although multiple organs are known to be affected by the disease, pulmonary involvement should be considered the most significant, as it is associated with a higher risk of relapse. A wide variety of hepatic complications are also reported. However, cholestasis has only been reported in a few cases. The pathophysiology of liver dysfunction due to typhoid infection has not yet been fully understood. Evidence of whole *Salmonella typhi* in the liver tissue of patients with typhoid fever shows that there is an interplay of microorganism associated factors and immunity that causes liver injury [7]. HEV is a self-limiting, waterborne, or enterically-transmitted acute viral hepatitis. HEV is an icosahedral, non-enveloped single-stranded RNA virus that is structurally like viruses in the Hepeviradae family. Infection of symptomatic HEV is most likely in young adults who

are 15 to 40 years old. Considering that HEV and *Salmonella typhi* have a common route of transmission, the co-infection has been reported uncommonly [8]. When HEV-infected patient complains of fatigue, or symptoms like vomiting, tiredness, fever, and stomach pain, it shows liver involvement [9]. Increasing numbers of HCV and HEV co-infection have been reported in recent literature, most of them in young adults in regions endemic to the virus [10]. Pakistan has an extremely high prevalence of HCV, undergoing a historical ratio of one infected in every 20 Pakistanis [11]. Our patient was suspected of malaria as well because of symptoms like high temperature, feeling hot and shivery, headaches, vomiting, muscle pains, and diarrhea. It is estimated that 300 to 500 million people acquire malaria each year, resulting in 1.5 to 2.5 million deaths annually [12]. The patient had oral thrush, which is not a serious problem normally, but the patients with a weakened immune system might experience the severity of the disease. Along with all these complications patient was continuously experiencing uneasiness in the stomach, nausea, and vomiting. The patient was suspected of HIV as well but unfortunately, these tests were never performed. The literacy rate in Pakistan is 62.3% with far lower numbers in the rural population, which contributed to his family making uninformed decisions [13]. With our total GDP per capita being 1,193.73 USD, and a lack of public sector funding for poor families, many such cases are seen routinely [14]. In our case, as presented, typhoid, HCV, and HEV infections contribute to treatment challenges, but due to failure in proper treatment, timely and accurate diagnosis, and poverty, lead to death.

Conclusion

It is particularly important to diagnose multiple infections in a single host in and timely. There were several specific tests requested but were never provided for by the caretakers, with reasons varying from financial constraints to distrust in the health care facility and physician, to extremely lower literacy levels in rural areas resulting in blatant incompliance. The patient was removed from the hospital majorly due to a lack of affordability on his family's behalf, while he needed intensive care and proper diagnosis. The current government is trying to improve the condition by providing health care donations and "Sehat Insaf Cards" (health insurance), but public awareness and education in rural areas still need to be addressed resolutely.

Authors contribution

MAK, KA, SS, SS, and MK have collected the data, RN and AA have written the manuscripts, SA has revised the manuscript, SA is the reporting physician, RN, MS, and UM have supervised the study.

Acknowledgment

We are thankful to the late patient and his family for allowing us to report this case and shed light to poor health care conditions in our country.

Conflict of interest

The authors declare no conflict of interest.

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