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Into the Enteric Verse Fighting Metabolic Acidosis

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Abstract: ***Enteric fever is an acute infectious disease caused by Salmonella Typhimurium and Salmonella Paratyphimurium. There is a high incidence of 100-1600 cases per 100000 cases annually in South-Asian countries like Nepal. A few cases of complications of enteric fever such as metabolic acidosis, sepsis and Acute Respiratory Distress Syndrome (ARDS) have been reported. Here, we report a case of 18-year-old male with typical features of blood and stool culture positive enteric fever who developed sepsis and metabolic acidosis while being treated with oral antibiotics during his course of illness. Examination showed raised temperature, low blood pressure, diffuse crepitation on chest auscultation and collapsed inferior venacava (IVC) on bed side ultrasonography (USG). Patient was then treated in Intensive Care Unit (ICU) with intravenous antibiotics and other supportive treatment for total of seven days. At the time of discharge, patient was afebrile and there was no growth on blood and stool culture***

Keywords: Antibiotics, Blood and Stool Culture, Metabolic Acidosis, Sepsis

1. Introduction

Enteric fever is an acute infectious disease which is caused by *Salmonella* Typhimurium and *Salmonella* Paratyphimurium. Global estimation of enteric fever is 27 million cases annually [1].South Asian countries like Nepal have high incidence of 100-1600 cases per 100000 cases annually [2,3]. During the course of illness, complications such as- metabolic acidosis, sepsis, ARDS may arise [4]. There are few reported cases of such complications. Bone marrow culture is considered to be more sensitive (55-90%) than blood culture (40-80%). However, stool culture is found to be negative in 60-70% cases in first week and can become positive in the untreated patient in the third week [5] It is very important to know about the severe complications of enteric fever because if untreated it can lead to metabolic acidosis, sepsis and eventually death. Proper antibiotic therapy should be initiated as soon as possible to prevent severe complications of enteric fever and reduce in a case fatality rate to less than 1% [5].

2. Case Presentation

Eighteen years old thin built male from Arghakhanchi (Western Nepal) came to the fever clinic with chief complaint of fever for seven days which was associated with chills and rigor. There was no documentation of temperature. He also complained of dry cough for five days and loose stool for three days. There was also history of few episodes of vomiting, anorexia and abdominal pain.

On examination, the patient was thin built and ill looking. His vitals were: Temperature-101.6◦ F, respiratory rate (RR)-20/minute and blood pressure (BP)-100/70 mm Hg, pulse rate-102/minute (regular) and Spo2- 98% at room air. His other systemic examination revealed no abnormalities. After sending the necessary investigations, he was enrolled in NUFIT (Nepal undifferentiated febrile illness trail) study [6] with provisional diagnosis of enteric fever. He was prescribed with oral cotrimoxazole along with oral rehydration solution (ORS) and paracetamol.

He came for follow up in the outpatient clinic on the second day of enrolment to the study where he was found to be in respiratory distress. During that visit, temperature-100.8 ◦ F, RR was 30/minute, BP was 80/50 mm Hg and pulse rate was 88 /minute (regular) and Spo2 was 98% at room air. After fluid resuscitation with one liter of normal saline (NS), he was again assessed and found to be tachypneic with RR fluctuating from 40-50 per minute. His chest examination revealed diffuse mild crepitation. Bedside ultrasonography revealed collapsed IVC. Provisional diagnosis of enteric fever with sepsis was made following which intravenous antibiotics and fluids were initiated and patient was transferred to ICU for further management.

During admission, arterial Blood Gas (ABG) analysis revealed compensated metabolic acidosis with pH of 7.36 (7.35-7.45), pCO2 of 25.7 mm Hg (35-45 mm of Hg), bicarbonate of 14 mmol/L (22-28 mmol/L) and anion gap of 18.8 mmol/L (12-18 mmol/L). Echocardiography and Chest X-ray revealed no abnormalities. Serology for hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV (human immunodeficiency virus) 1 and 2 were negative. Routine urine examination and culture reports were normal. In blood and stool culture, *Salmonella*Typhimurium was isolated which was sensitive to ampicillin, azithromycin, ceftriaxone, chloramphenicol, ciprofloxacin and cotrimoxazole but resistant to nalidixic acid. Admission laboratory findings are summarized in Table 1.

Table 1: Laboratory values at the time of admission

Laboratory findings	Results	Normal Range
WBC	3.8×10^3/uL	$4.5\text{-}11.0\times10^3$/uL
Hemoglobin	14.7g/dL	13.2-17.5 g/dL
Creatinine	0.9mg/dL	0.61-1.24 mg/dL
AST	314 U/L	10-60 U/L
ALT	172U/L	38-126 U/L
Sodium	128mmol/L	136-145 mmol/L

Potassium	4.5mmol/L	3.5-5.2 mmol/L
Lactate	3.1 mmol/L	0.5-1 mmol/L

Patient was managed with fluid, antibiotics (Inj. Ceftriaxone 2g IV OD, Inj. Azithromycin 1gm OD, Inj. Vancomycin 1 gm BD) and Inj. Heparin 5000 I.U for DVT prophylaxis which was continued for seven days. Gradually, his ABG profile normalized and vitals were stable: BP-110/70 mm Hg, RR- 22/min, temperature-98◦ F, pulse rate-76/min and Spo2 was 97% at room air following which he was discharged. Blood and stool culture report during the follow up showed no growth. Discharge laboratory findings are summarized in Table 2.At the time of discharge, blood and stool culture showed no growth of *Salmonella* Typhimurium.

Table 2: Laboratory values at the time of discharge

Laboratory findings	Results	Normal Range
WBC	6.8×10^3/uL	$4.5\text{-}11.0\times10^3$/uL
Hemoglobin	11.2 g/dL	13.2-17.5 g/dL
Creatinine	0.7 mg/dL	0.61-1.24 mg/dL
AST	68 U/L	10-60 U/L
ALT	215 U/L	38-126 U/L
Sodium	128mmol/L	136-145 mmol/L
Potassium	4.5mmol/L	3.5-5.2 mmol/L
CRP	222mg/L	0-10 mg/L

3. Discussion

This patient presented after seven days of onset of fever and developed atypical manifestations like fully compensated metabolic acidosis and sepsis during the course of treatment with oral antibiotic. Tachypnea can be explained by respiratory system compensating for metabolic acidosis. Although diffuse crepitation were heard in all areas of chest which suggests enteric pneumonitis but chest X-ray was reported to be normal. According to a study conducted by Dutta, T. and Ghotekar, L there were more incidences of multiple atypical presentation in late entry group than early entry group (cut off three weeks). Although our patient falls under early entry group however in clinical practice seven days is a long time to be left untreated for enteric fever. Atypical presentation didn't lead to poor prognosis in the study [7].

In a similar reported case of culture proven enteric fever in U.S the patient, with no history of travel, presented within two days of becoming symptomatic had worsened course of illness than our patient. This patient developed fulminant ARDS, septic shock and required endotracheal intubation and mechanical ventilation [8]. A cross-sectional study compared serum bactericidal antibody (SBA) assay in different age group of participants of Nepal (endemic) with than of UK (not endemic) [9]. The study excluded people with history of typhoid fever or vaccination. This study showed that the SBA increased with age in participant from Nepal whereas it remained low in participants from UK in all age groups. Since U.S being non endemic area like U.K it's fair to assume the SBA from participants from U.S would have followed similar course. SBA level correlates with the decreased incidence of disease with increasing age group in endemic areas. High level of SBA in our patient might be a key factor in advent of the disease in comparison to the patient from US. This also shows the usefulness of vaccines to decrease susceptibility to enteric fever and severe infection since vaccines increase SBA level [9].

Our patient showed classical signs of enteric fever and also found to have stool culture positive for *Salmonella* Typhimurium taken in seventh day of illness which is usually negative in 60-70 % of patients and usually positive in third week of illness in untreated patients [5]. Although most cases of enteric fever has an indolent course [10], we should always be vigilant because it can cause grave consequences.

4. Conclusion

Usually, enteric fever has indolent course and responds well to antibiotic therapy. However, it can lead to atypical complications such as sepsis and metabolic acidosis despite treatment in few cases. People from non-endemic areas can be at risk of severe infection than those from endemic areas. Availability of point of care diagnostics can be useful to quickly diagnose enteric fever and commence treatment. Blood and stool culture are very important and specific investigations for enteric fever. Multiple atypical complication of enteric fever doesn't necessarily mean poor prognosis.

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