

From Gut to Heart: Extensively Drug-resistant *Salmonella typhi* with Multi System Involvement

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ABSTRACT

Extensively drug-resistant (XDR) *salmonella typhi* is a gram-negative bacillus, transmitted by feco-oral route. Its systemic manifestations are protean. Untreated enteric fever carries high morbidity and mortality. Life-threatening complications are mainly extra-intestinal, and include involvement of central nervous system, lungs, liver, and genitourinary system. We report a case of a young girl presenting to a hospital in Karachi with a 1-week history of fever, rigors, abdominal pain, watery diarrhea, nausea, and anorexia. She developed toxic myocarditis, pulmonary edema, septic shock, and coagulopathy. Multi-drug-resistant (MDR) *salmonella typhi* was isolated from blood cultures. Her symptoms resolved after intravenous antibiotics and she completely recovered.

Key Words: Myocarditis, *Salmonella typhi*, Coagulopathy.

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INTRODUCTION

Typhoid is endemic in Pakistan and presents as enteric fever with systemic involvement.¹ With the resistance of antibiotics and poor hygiene in metropolitan cities, enteric fever remains endemic and presents with uncommon manifestations.¹ The causative pathogen can rarely cause myocarditis.² The association of myocarditis with *salmonella typhi* was first described in 1884.¹ Local data for enteric fever-induced cardiac complications is scarce. Cases reported in literature showed *salmonella typhi* in blood cultures. The resistant strains are a challenge to treat; hence, the need to choose antibiotics carefully. Electrocardiograms and electrolytes should be carefully monitored during the course of treatment. More case reports regarding enteric fever and its extra-intestinal manifestations will be useful for emergency physicians and other clinicians.

CASE REPORT

A 22-year girl, with no known comorbidities, presented to the Emergency Room with fever and episodes of loose stools and vomiting. Fever started two weeks back, was of high grade (documented upto 103°F), with rigors and chills.

Fever was continuous, lasted throughout the day and partially relieved with antipyretics, but recurred after two to three hours. It continued for three days and then subsided. There were no associated cough, sore throat, chest congestion, urinary or bowel symptoms. There was no history of travel. Oral amoxicillin was started and workups for fever, including malarial parasite (MP) and immunochromatographic test (ICT) for malaria, were carried out, which were negative. Dengue antigen was also negative. On day-7, fever recurred and it was associated with loose watery stools, small in quantity, about three to four episodes per day, contained no blood, associated with abdominal cramps and nausea. Blood cultures were drawn and enteric doses of ceftriaxone were administered empirically by the primary physician. After four days, provisional reports of blood culture showed extensively drug-resistant (XDR) *salmonella typhi*, which was sensitive to imipenem and azithromycin only. The patient was switched to intravenous imipenem; however, the frequency of stools increased to eight to nine episodes per day, with associated nausea and three episodes of vomiting; hence, the patient was brought to Emergency Room.

On arrival, the patient appeared ill but oriented. She was hypotensive and tachycardiac, with blood pressure of 80/40 mmHg and a heart rate of 123 beats/minute. Respiratory rate was 28 breaths per minute, oxygen saturation 96 % on room air, and temperature of 38.5°C (101.3°F). She was pale-looking; however, there was no evidence of cyanosis, clubbing, lymphadenopathy and edema. No jaundice was found. The systemic examination was unremarkable.

Laboratory workup revealed hemoglobin of 8.3 g/dL, total leukocyte count 3,100/uL, and platelets 38000/uL. Blood tests were notable for hyperbilirubinemia (total bilirubin 4.2 mg/dl) with elevated transaminases and hypokalemia (3.6 mmol/L). Procalc-

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tonin was elevated (33.64 ng/ml). Fibrinogen degradation products were elevated (>20 ug/ml), with fibrinolysis lag-times (FLT) 358 sec, and D-dimers > 30 mg/dl. Electrocardiogram (ECG) revealed sinus tachycardia, with diffusely flattened T waves. Initial chest X-ray showed hilar vascular congestion consistent with pulmonary edema.

The management was started as complicated enteric fever with septic shock, disseminated intravascular coagulation (DIC) with coagulopathy and hypokalemia. Antibiotics were switched to meropenem and azithromycin. After fluid resuscitation, she was started on norepinephrine infusion, and potassium replacement was initiated. Due to suspicion of infective endocarditis, transthoracic echo was performed, which showed ejection fraction (EF) of 30% with moderate to severe global hypokinesia. There was moderate to severely-reduced left ventricular systolic function with no evidence of vegetations or clots. However, the patient denied any prior history of exertional shortness of breath, orthopnea, functional limitation due to shortness of breath, spells of cyanosis during childhood, family history of cardiac disease and reported normal functional activity as well as routine participation in sports activities with no functional limitation. Cardiology input was taken; and reduced left ventricular systolic function was presumed to be due to myocarditis, related to enteric fever. The patient gradually improved clinically and inotropic support was gradually tapered. She remained clinically stable and was discharged to continue antibiotics at home. Upon clinic follow-up after one week, the patient reported significant clinical improvement and was able to resume her routine activities. A review echocardiogram, done two weeks post-discharge, showed improved EF to 50%, with mildly reduced left ventricular systolic function as compared with moderate to severely- reduced left ventricular systolic function during admission.

DISCUSSION

This was a case of severe enteric fever with myocarditis due to XDR *salmonella typhi* infection, which is very rarely reported in the literature.¹ Fever showed stepped escalation with prolonged plateau phase, denoted by the term Wunderlich's curve.² The use of combination therapy with Imipenem and azithromycin appeared to be highly effective.³

Life-threatening complications of typhoid fever include involvement of the gastrointestinal system, central nervous system, cardiovascular system, pulmonary system, bone and joints, hepatobiliary system and genitourinary system.²⁻⁵

Cardiovascular complications with enteric fever include myocarditis, endocarditis, pericarditis and arteritis.³ Literature reports myocarditis in approximately 4% to 7% of patients with enteric fever.²⁻⁵ Prabha *et al.* reported 7% of patients with enteric fever-induced myocarditis with 46% of patients having transient ECG changes. ECG abnormalities were QTc prolongation (29%), ST-T changes (20%), bundle branch block (7%), first degree A-V block (2%), and arrhythmias (2%).⁴

Al-Aqeedi *et al.* reported a case of a 34-year gentleman from India who travelled to Qatar. He presented with fever, which led to multi-organ failure. His cardiac complications were myocarditis with pulmonary edema.⁶ Arrhythmias with ventricular fibrillation could be due to hypokalemia with reduced EF. The cardiac dysfunction could be the direct result of enteric fever and may be due to endotoxin release.⁶⁻⁹ The endotoxin can cause cardiovascular collapse and mortality among this group of patients. It is important to note that serial ECG and electrolyte levels should be closely monitored.

PATIENT'S CONSENT:

Verbal consent from the patient was taken.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

SS, UJ: Drafted and edited the manuscript.

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