

Hemolytic Anemia - A Rare Presentation of Enteric Fever

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Abstract: 17 year old male patient presented to casualty with the chief complaints of fever, pain in abdomen, yellowish discoloration of skin and sclera since 5 days. On investigation he was found to have jaundice, acute kidney injury, with hemolytic anemia. His HIV, HBsAg, HCV, HAV, HEV, sickling, peripheral smear for MP and Malarial antigen, coombs test and G6PD deficiency were all negative. Widal test for enteric fever was strongly positive. He was treated on line of enteric fever with antidiotics and supportive treatment. With the treatment, he improved clinically and laboratory investigation also showed rapid improvement. He was discharged on 8th day with improved sign and symptoms. After 15 days he was fully recovered and asymptomatic.

Keywords: enteric fever, hemolytic anemia

1. Introduction

Enteric fever is an acute systemic infectious disease caused by *Salmonella typhi* which affects only humans.¹ *Salmonella typhi* is a gram negative rod which lives and grows in mononuclear phagocytic cells of the reticuloendothelial tissue.² It usually spreads by oral-fecal route from patients with typhoid fever or carriers. Despite wide availability of effective antimicrobial agents, typhoid fever remains an important public health problem. It is eminently present worldwide with higher prevalence in developing countries. Due to improvement in food hygiene and use of water/sewage treatment, incidence of enteric fever has markedly reduced in developed part of the world. However, there are still an estimated 27 million cases of enteric fever in the world with 200, 000–600, 000 deaths annually. The annual incidence is highest (>100 cases/100, 000 population) in south-central and Southeast Asia; medium (10–100 cases/100, 000) in the rest of Asia, Africa, Latin America, and Oceania (excluding Australia and New Zealand); and low in other parts of the world³

Most common complaints in patients of enteric fever are fever, chills, headache, abdominal pain, constipation or diarrhea. It is a severe disease with many other varieties of complications,⁴ including meningitis,⁵ psychosis,⁶ pneumonia,⁷ myocarditis,⁸ hepatitis,⁹⁻¹² pancreatitis,¹³⁻¹⁶ nephritis^{12, 17} and osteomyelitis,¹⁸. Gastrointestinal bleeding (10-20%) and perforation (1-3%) are also seen rarely. However, hemolytic anemia is rarely seen in patients with enteric fever. We report a case of a patient with typhoid fever who presented with hemolytic anemia.

2. Case Report

A 17 year old male patient from rural area, presented in casualty with complaint of moderate fever since four days, associated with mild headache, chills and rigors. Fever was

intermittent with 2-3 episodes/day but there was no diurnal variation. He also complained of anorexia and generalized weakness with easy fatigability since three days. He also gave a history of yellowish discoloration of sclera and urine since two days associated with right sided abdominal pain and black colored stool. There was no history of vomiting, loose stool, joint pain, chest pain or breathlessness.

On general examination patient was afebrile with pulse rate-100/min regular, B.P was 80/60 mmHg and Respiratory rate was 22/min. He had severe pallor and icterus. On systemic examination there was tenderness in the right hypochondrium and hepatomegaly was present. Examination of other systems was normal.

On investigating, complete blood count revealed hemoglobin level of 5 g/dl, leukocyte count 18000/mm³ with predominant neutrophils and platelet count 295000/mm³ and erythrocyte sedimentation rate (ESR) 86. Urinalysis showed mild proteinuria, blood urea nitrogen (BUN) was 332 mg/dl and serum creatinine was 5.1 mg/dl. Total bilirubin was 12.6mg/dl with direct reacting bilirubin 7.1 mg/dl. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and Alkaline phosphatase were 92 U/l, 169 U/l and 307 U/l (check units) respectively. He had Retic count- 6%, S. iron-196 mg/dl, S. ferritin-904 ng/dl, total iron binding capacity (TIBC)-458 mg/dl. Peripheral smear showed mild anisopoikilocytosis, target cells, polychromatic RBCs with leukocytosis and adequate platelets and no blood parasite. The occult blood test of stool was positive. Lactic dehydrogenase (LDH) was 3925 U/l, prothrombin time (PT) was 17.8s (control 14s) with INR-1.27 and activated partial thromboplastin time (APTT) was 30 s (control 30 s). HIV, HBsAg, HCV, HAV, HEV, sickling, peripheral smear for MP and Malarial antigen, coombs test and G6PD deficiency were all negative. His Widal test showed S.Typhi (O) and (H) titres-1:320. USG showed hepatosplenomegaly and gall bladder sludge. His UGI scopy revealed multiple distal esophageal ulcers.

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Based upon clinical and laboratory examination, a diagnosis of enteric fever with esophageal ulcers with Acute renal failure with hemolytic anemia was made. He was given inj. Ceftriaxone 2gm iv 12 hourly and tab azithromycin 500mg od along with other symptomatic and supportive treatment. He also received 2 units of packed cell volume.

The patient responded well to the treatment with visible improvements in lab reports on day 4 and day 6 (table 1).

Table 1: Lab reports on 1st, 4th and 6th day of admission.

DAYS	1 st	4 th	6 th
Hemoglobin (mg/dl)	5	7.3	8.5
TLC (per cumm ³)	18000	16,000	10,700
Platelets (per cumm ³)	295000	279000	260000
S. Bilirubin (mg/dl)	Total-12, Direct -7.1	Total - 4.2	Total -2.5
SGPT (U/l)	169	869	400
SGOT (U/l)	72	581	97
S. creatinine (mg/dl)	5.1	1.5	0.9
B. Urea (mg/dl)	332	127	36

Patient was discharged on 8th day after admission, with improved signs and symptoms as well as laboratory investigations. After 15 days of discharge he was asymptomatic with normal vitals and no fresh complaints.

3. Discussion

S. Typhi is a Gram-negative bacillus that invades small bowel and causes typhoid fever. Acquired through feco-oral route, the bacillus invades small intestinal mucosa and reaches the reticuloendothelial cells through lymph and blood. They reside in the reticuloendothelial system for many days, multiply and cause recurrent episodes of bacteremia to infect various organs. This is the symptomatic phase which is marked by hyperplasia of the lymph nodes, liver and spleen. The terminal ileum of gastrointestinal tract is predominantly involved due to presence of abundant lymphoid follicles (Peyer's patches) which undergo hyperplasia and may subsequently ulcerate.

Clinical presentation and severity of the disease is varied. Fever, headache, flu-like symptoms, fatigue, nonproductive cough, loss of appetite, nausea and myalgia are the most frequent symptoms^{2, 19}. It lasts for around four weeks. First week of illness is marked by high fever, toxemia and constipation while diarrhea is mostly seen in the second week. Most of the complications develop in the third and fourth weeks of the infection if left untreated¹. The most common complications encountered are intestinal hemorrhage, perforation, toxic myocarditis, bronchitis and toxic confusion due to enteric encephalopathy, but it may affect almost all systems¹. Complications like splenomegaly, bone marrow findings, encephalopathy, intestinal hemorrhage and perforation are typically seen in the third week^{19, 20}. However, our patient had a rapidly progressive course of illness. He had a total history of only five days. Most complications like jaundice and gastrointestinal bleeding started within three days of onset of fever. He presented to us on fifth day of onset of fever and had already developed intestinal ulcers with bleeding, jaundice and acute renal failure. Hemolytic anemia is a very rare complication of enteric fever. In our case, patient

developed hemolytic anemia also along with the other complications. Another notable feature is that with prompt diagnosis and management the recovery was equally rapid.

In summary, this case highlights the potentially serious complications of hemolytic anemia with multiple organ involvement in typhoid fever. It also brings to notice the rapidly progressive course that enteric fever can take and the equally rapid response that can be seen if diagnosed soon and treated appropriately. Thus, enteric fever should also be considered as a differential diagnosis of hemolytic anemia. Early recognition, together with supportive and adequate antimicrobial treatment are mandatory for these patients.

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