# An uncommon presentation of enteric fever: Cholestatic Hepatitis

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***Abstract-*** Enteric fever (EF or typhoid) is a common infectious disease. It is a common cause of morbidity and hospital admission in developing countries like India. We report a case of Cholestatic Hepatitis secondary to enteric fever in a 42-year-old male who was admitted to our medical emergency unit with chief complaints of fever for 9 days followed by anorexia, abdominal discomfort and jaundice. He recovered completely to prompt administration of appropriate antibiotic therapy with supportive management.

***Index Terms***- Enteric Fever, *salmonella,* Cholestatic jaundice, Icterus, *salmonella* hepatitis

## I. Introduction

Enteric Fever is a systemic disease characterized by fever, abdominal pain and caused by dissemination of *S. typhi or S. paratyphi* which is pathologically as a unique illness because of its association with enlarged Peyer's patches and mesenteric lymph nodes.[1] The Gastrointestinal complications of EF are intestinal haemorrhage and perforation, acute pancreatitis, hepatic abscess, acute cholecystitis, splenic rupture and hepatitis.[2] Liver tests suggesting cholestatic disorder may be due to intra- or extrahepatic cholestasis. EF is known to cause a wide range of hepatic complications.[3] However, only few cases of cholestatic hepatitis secondary to EF are reported in literature.[4,5]

## II. Case Report

A 45 years old male, office worker, resident of lucknow was presented in our emergency department with chief complaints of anorexia, and high grade fever for 12 days followed by a vague right hypochondrial discomfort, vomiting and yellowish discolouration of eyes for 4 days. On enquiry he told that he had also constipation associated with dark urine. He denied complaint of pruritus. He had no history of jaundice, alcoholism, contact history with muddy water and blood transfusions, promiscuity or intravenous drug abuse and significant past medical history.

On general examination patient was conscious and well oriented. He had icterus. He had no pallor or lymphadenopathy. He was febrile (103°F) and his pulse rate was 90/ min and regular, B.P-110/80mmHg and respiratory rate was-19/min. Systemic examination revealed tender firm mild hepatomegaly and gall bladder was not palpable. Rest of the systemic examinations were within normal limit. Investigations of patient during hospitalisation are summarised in table 1. Computerized tomography (CT) of abdomen showed mild hepatomegaly (15.8cm) with normal margins and normal CT attenuation value. No evidence of any intrahepatic biliary radical dilatation (IHBRD) noted. Gall bladder is noted to be distended with normal in CT attenuation value with normal wall thickening.[Figure1] Liver biopsy showed hepatic cholestasis [Figure2]. Enzyme-linked immunosorbent assay for human immunodeficiency virus, Australia antigen for Hepatitis B and antibody against Hepatitis C virus were negative. Serology (IgM antibody) for dengue infection and smear examination for malarial parasite were negative. Electrocardiography and chest X-ray were within normal limit. His blood culture was sterile and serology (IgM antibody) for *Salmonella typhi* was positive. Our case was already on oral antibiotic at the time of admission which could be a reason for sterile blood culture. The diagnosis of cholestatic hepatitis due to enteric fever was made on the basis of clinical and laboratory parameters with positive serology (IgM antibody) for *Salmonella typhi.* So ceftriaxone 3gm per day intravenous was started for 10 days. Patient was started improving day by day and got discharged on 12$^{th}$ day of admission. Liver function test showed near normalization on follow up after 2 weeks of admission.

## III. Discussion

Enteric fever remains a serious health threat in developing countries including India.[6] Most commonly, food-borne or waterborne transmission results from fecal contamination by ill or asymptomatic chronic carriers. Up to 10% of untreated patients with typhoid fever excrete *S. typhi* in the feces for up to 3 months, and 1–4% develop chronic asymptomatic carriage, shedding *S. typhi* in either urine or stool for >1 year which increases its prevalence and incidence. Enteric fever can manifest a variety of systemic complications ranging from mild to life-threatening such as gastrointestinal bleeding and intestinal perforation which most commonly occur in the third and fourth weeks of illness.[1] Rare complications whose incidences are reduced by prompt antibiotic treatment include disseminated intravascular coagulation, hemophagocytic syndrome, pancreatitis, hepatic and splenic abscesses and granulomas, endocarditis, pericarditis, myocarditis, orchitis, hepatitis, glomerulonephritis, pyelonephritis and hemolytic uremic syndrome, severe pneumonia, arthritis, osteomyelitis, and

parotitis.[7,8] The first case of hepatic involvement in typhoid fever was reported by William Osler in 1899.[9] Pramoolsinsap *et al*. in their comprehensive review of Salmonella hepatitis suggested that typhoid fever is often associated with abnormal liver biochemical tests, but severe hepatic involvement with clinical features of acute hepatitis is a rare complication.[10] Liver involvement in enteric hepatitis may be in the form of hepatomegaly alone, jaundice, biochemical alterations and histopathological changes.[3] The possible associated factors for development of salmonella hepatitis are virulence of the organisms, delayed treatment and poor general health of the patients.

The exact pathogenesis of severe hepatic involvement in salmonella infection is not fully known and needs further studies. Though endotoxin, local inflammatory and/or host immune reactions may be responsible for development of hepatitis in salmonella infection.[11] Our case had isolated hyperamylasemia and hyperlipasemia without evidence of pancreatic involvement. This may be possible as result of a reduced excretion due to either impaired renal or liver function which is common in Salmonella infections.[12]

The common causes of intra- hepatic cholestasis are Viral hepatitis (Hepatitis A, B and C, Epstein-Barr virus, cytomegalovirus), Alcoholic hepatitis, Drug toxicity (anabolic and contraceptive steroids, chlorpromazine, erythromycin estolate, prochlorperazine), Primary biliary cirrhosis, Primary sclerosing cholangitis, Chronic rejection of liver transplants, Sarcoidosis, Inherited, Cholestasis of pregnancy, Total parenteral nutrition, Nonhepatobiliary sepsis, Benign postoperative cholestasis, Paraneoplastic syndrome, Venoocclusive disease, Graft-versus-host disease, Infiltrative diseases like TB, Lymphoma, Amyloid and infections like Malaria, Leptospirosis.[13] All the causes of cholestasis were ruled out with the help of clinical examination and investigations. We are reporting this case because the patient recovered completely after starting of Enteric Fever therapy which also supports our final diagnosis of cholestatic hepatitis secondary to enteric fever.

## IV. Conclusion

With the above description it is clear that enteric fever can causes a variety of systemic manifestations in endemic countries. Cholestatic hepatitis should be kept in mind as a differential diagnosis in patients of enteric fever complaining of jaundice at peak of fever. Early diagnosis and management with prompt supportive care improves prognosis in these cases.

**Table 1; Patient's laboratory parameters**

| Laboratory parameters | | Duration from admission | | | | | |
|---|---|---|---|---|---|---|---|
| | Normal range | 1st day | 4th day | 8th day | 2nd week | 4th week | 6th week |
| Hb(g/dl) | 13-17 | 12.2 | 11.2 | 10.8 | - | - | - |
| TLC (103/µL ) | 4-11 | 9.2 | 12.6 | 8.0 | - | - | - |
| DLC (%) | N40-80 L20-40 | N78L09 | N80L15 | N67L22 | - | - | - |
| PC (103/µL ) | 140-440 | 188 | 165 | 200 | - | - | - |
| S.Na+(mmol/L) | 135-155 | 134 | 137 | 138 | - | - | - |
| S.k+(mmol/L) | 3.5-5.5 | 3.5 | 3.8 | 3.4 | - | - | - |
| S.Urea(mgdl ) | 20-40 | 49.4 | 29.5 | - | - | - | - |
| S.Creat (mgdl ) | 0.5-1.2 | 0.95 | 0.7 | - | - | - | - |
| RBS(mg/dl) | 70- | 112 | 112 | - | - | - | - |
| PT(seconds) | 10.4-12.6 | - | 13.9 | - | - | - | - |
| INR (seconds) | 0.8-1.2 | - | 1.21 | | - | - | - |
| S.Bilirubin-Direct | 0.0-1.1 | 12 | 13 | 10 | 6 | 3 | 0.8 |
| S.Bilirubin-Indirect | 0.0-0.3 | 1.5 | 2 | 2 | 1 | 0.8 | 0.2 |
| ALT (IU/L) | 21-72 | 300 | 375 | 199.6 | 150 | 70 | 66 |
| AST (IU/L) | 17-59 | 200 | 225 | 72.6 | 70 | 42 | 42 |
| S.ALP | 38-126 | 2100 | 2000 | 1400 | 800 | 302 | 120 |
| S.Protein(g/dl) | 6.3-8.2 | 7.4 | 7.2 | 8.0 | - | 7.4 | - |
| S.Albumin(g/dl) | 3.5-5.5 | 3.4 | 3.5 | 4.6 | - | 4.0 | - |
| S. Amylase(U/L) | 22-80 | 412 | - | 116 | - | - | - |
| S.Lipase(U/L) | Upto 60 | 302 | - | 100 | - | - | - |

ALT, alanine transaminase; ANA, antinuclear antibody; AST, aspartate transaminase, S.ALP, serum alkaline phosphatase; RBS, random blood sugar; PT, prothrombin time; INR, international normalised ratio.

## REFERENCES

[1] Pergues DA, Miller SI. Salmonellosis. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J et al., editors. Harrison's principles of internal medicine. 18th ed. New York:McGraw Hill; 2012, p1247-1280

[2] Koshi G. Uncommon manifestations of salmonella infections. Indian Journal of Medical Research. 1976;64(2):314-321

[3] Khosla SN: Typhoid hepatitis. Postgrad Med J 1990, 66:923-925

[4] Arabaci F, Irmak H, Akdeniz H, Demiröz AP: Jaundice with cholestasis: a case of typhoid hepatitis. Turkish Journal of Infection 2003, 17:99-102.

[5] Albayrak A, Gunbey SS, Aktas F: Cholestatic hepatitis due to Salmonella typhi. Clinics and Practice 2011, 1:e13

[6] Dutta S, Dipika S, Byomkesh M, Bhaswati S, Alok Kumar D, Jacqueline LD, John W, Lorenz VS, Leon O, John DC and Sujit Kumar B. Evaluation of new-generation serologic tests for the diagnosis of typhoid fever: data from a community-based surveillance in Calcutta, India. Diagnostic Microbiology and Infectious Disease 2006;56(4) 359-365

[7] Shetty AK: Typhoid Hepatitis in Children. J Tropical Ped 1999, (45):287-290.

[8] Gitlin N: Bacterial and systemic infections. In Disease of the liver. 8th edition. Edited by sciff's. Lippincott William and Wilkins; 1999:1549-58

[9] Osler W: Hepatic complication of typhoid fever. Johns Hopkins Hosp Rep 1899, 8:373-87

[10] Pramoolsinsap C, Viranuvatti V. Salmonella hepatitis. J Gastroenterol Hepatol. 1998;13:745–50

[11] Bhutta ZA, Elder JS, Kleigmen RM, Schor NF, Geme WST. Nelson Text book of Pediatrics. 19th ed. India; Elsevier: 2011

[12] Pezzilli R, Andreone P, Morselli-Labate AM, Sama C, Billi P, Cursaro C, et al. Serum pancreatic enzyme concentrations in chronic viral liver diseases. Dig Dis Sci.1999;44:350-355.

[13] Pratt DS, Kaplan MM. Jaundice. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J et al., editors. Harrison's principles of internal medicine. 18th ed. New York:McGraw Hill; 2012, p324-329

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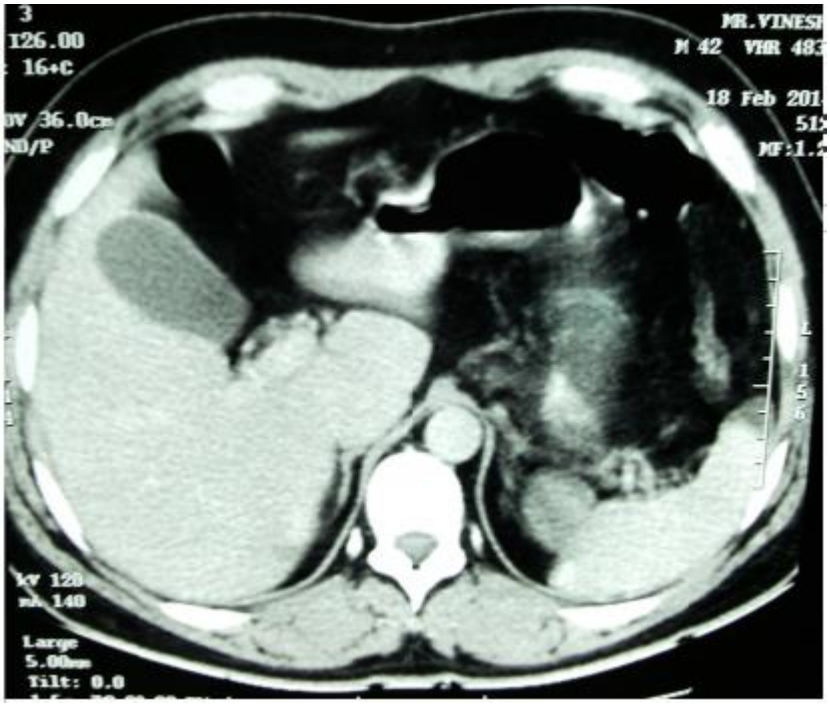


Figure 1: Computerized tomography (CT) imaging of abdomen showing mild hepatomegaly (15.8cm). No evidence of any intrahepatic biliary radical dilatation (IHBRD) noted. Gall bladder is distended with normal wall thickening

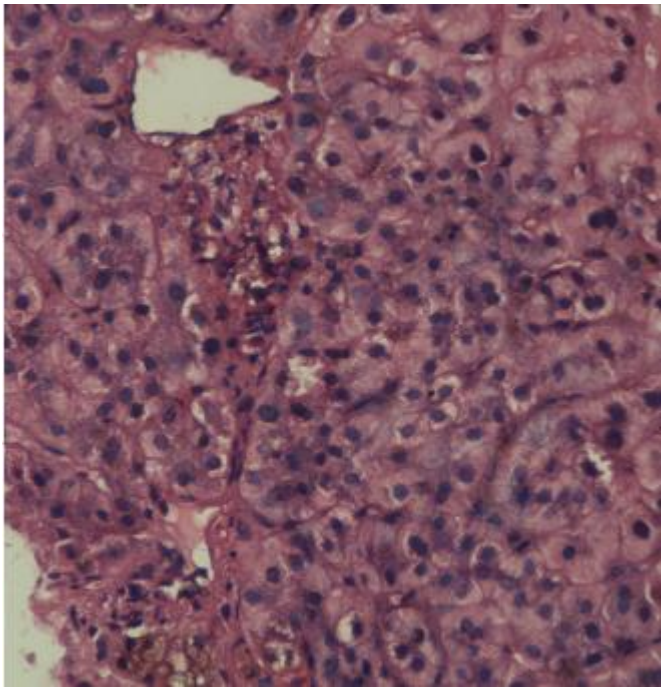

Figure 2: Liver biopsy showing hepatic cholestasis without inflammation.