

SALMONELLA HEPATITIS (ANALYSIS OF HEPATIC INVOLVEMENT IN 107 PATIENTS WITH TYPHOID FEVER)

M. Rasoolinejad*, N. Esmailpoor Bazaz and B. Mogbel Alhosein

Department of Infectious Disease, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract: Recognition of typhoid hepatitis is important since it has to be differentiated from other common ailments in our country such as viral, malarial or amoebic hepatitis. Early institution of specific therapy in cases of typhoid hepatitis carries a good prognosis. In our study, 107 patients with positive blood or bone marrow cultures for *Salmonella typhi*, were evaluated for hepatomegaly and abnormal serum liver enzymes, PT and alkaline phosphatase. The clinical features of typhoid fever with hepatic involvement include: fever 100%, hepatomegaly 52.3%, clinical jaundice 1.8%, rising in ALT 71.1%, AST 24.2%, Alkaline phosphatase 23.3% and abnormal PT 63.5%. Both clinical and biochemical abnormalities were seen in 22.4% of our patients. In patients with fever and jaundice with or without abnormality in liver enzymes, we must keep typhoid hepatitis in mind.

Acta Medica Iranica, 161-163; 2003

Key Words: *Salmonella typhi*, typhoid fever hepatitis, liver enzyme, liver function test

INTRODUCTION

Hepatic complications of typhoid fever were first reported by William Osler in 1899 (1). *Salmonella typhi* infection is still a major health problem in tropical and developing countries. It is uncertain whether salmonella bacteria produced hepatic dysfunction by direct invasion or by endotoxemia (2). The recent demonstration of intact *Salmonella typhi* in liver tissue of patients with typhoid fever suggests that organisms are phagocytosed by reticuloendothelial system but overcome the cell's killing action and produce hepatic injury by liberating cytotoxic substances in situ (3). The liver involvement ranges from mild elevation of aminotransferases and alkaline phosphatase for almost all patients during the second and third weeks of their illness to a picture indistinguishable from acute viral hepatitis (4,5). Liver biopsies demonstrate focal kupffer cell hyperplasia and mononuclear cell infiltration of the portal space (4). The kupffer cells tend to aggregate and the aggregations have been called typhoid nodules (2,6). The present study was designed to determine the clinical and hepatic biochemical alterations in the course of typhoid fever.

MATERIALS AND METHODS

A total of 107 patients with positive blood or bone marrow culture for *S. typhi* were studied with special attention to liver involvement. In every case, a detailed clinical history was taken and a thorough physical examination was performed with special attention to nausea, vomiting, right upper quadrant pain, hepatomegaly, jaundice, serum liver enzyme, bilirubin, prothrombin time (PT) and serum alkaline phosphatase. A diagnosis of typhoid hepatitis was made with fever, jaundice, hepatomegaly and rising in serum liver enzymes and when clinical and laboratory findings got improved after antibiotic therapy.

RESULTS

Out of population studied, there were 76 (71.1%) males and 31 (28.9%) females. The median age was 25.5 years (range 18 months to 67 years). All our patients were admitted to the hospital within the first 2 or 3 weeks of their illness. The symptoms and signs are summarized in table 1. Two patients were admitted with fever and jaundice, and 26 (24.2%) patients had jaundice on physical examination. Anemia was seen in 85 (79.4%), normal white blood cells in 90 (89.1%), leukopenia in 12 (11.2%) and thrombocytopenia in 10 (9.1%). Biochemical abnormalities in the form of raised serum bilirubin in 26 (24.2%), 2 to 30 folds rise in alanin transaminase (ALT) in 76 (71.1%) patients, 2 to 22 folds rise in aspartate transaminase (AST) in 56 (52.3%) patients were seen. The serum alkaline phosphatase level was high in 25 (23.3%) patients.

Received: 15 October 2002, accepted: 16 April 2003

*** Corresponding Author:**

M. Rasoolinejad, Department of Infectious Disease, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 6929216
Fax: +98 21 6929216
E-mail: mehrnaz_rn@yahoo.com

Salmonella hepatitis

Abnormal serum prothrombin time was noted in 68 (63.3%) patients. HBsAg test was performed in 15 (14.1%) patients and all of them were negative. We did not perform liver biopsy in our patients. Forty nine patients (45.7%) had normal clinical findings and normal liver enzymes, 58 patients (54.2%) had only liver enzymes rising and 24 (22.4%) patients had clinical findings abnormalities and liver enzymes rising.

Table 1. Clinical data of patients with typhoid fever

	No	%
Symptoms		
Headache	107	100
Fever	107	100
Nausea/vomiting	32	29.9
Anorexia	85	79.9
Abdominal pain	70	65.4
Diarrhea	25	23.3
Epistaxis	20	18.6
Jaundice	2	1.8
Signs		
Fever	107	100
Abdominal tenderness	70	65.4
Hepatomegaly	56	52.3
Splenomegaly	58	54.2
Jaundice	26	24.2
Rose spots	26	24.2
RUQ tenderness	20	18.2

Serial evaluation of physical examination and biochemical parameters showed return to normal level after recovery from acute illness in all cases.

DISCUSSION

Since the earliest description of hepatic involvement in typhoid by Osler who documented enlarged tender liver with clinical jaundice in 8 out of 1500 cases of typhoid fever, a number of studies have been reported. Hepatomegaly has been reported in 25-44% cases (3,7), however, we observed it in 56 (52.3%). Right upper quadrant tenderness and hepatomegaly was observed in 20 (18.6%) of our patients. It has been reported in 4.8% of patients in the study of Mathiew et al. (8). We observed hepatomegaly in all cases of jaundice in typhoid as Osler described (1). Ayhan et al (9), in a study of 16 cases of typhoid, found jaundice in none. Morgestern et al. (7) in their study of 20 cases of typhoid found jaundice in 9%, Gillin (3) reported 33% of 27 patients

with hepatitis who had jaundice. In our study, the presenting symptom of 2 patients was fever and jaundice. Abnormal biochemical tests suggestive of hepatic involvement have been reported in 23% of patients during first to third weeks of disease (7). Morgenstern et al. (7) believed that liver involvement is invariably present after the first week, in our study liver involvement was seen in 58 (54.2%) during the second and third weeks. The alkaline phosphatase level rose in 25 patients (23.3%), in Brandborg et al. (6) study alkaline phosphatase rising was more and in Miller et al. (4) was less prevalent. Rise of ALT and AST more than 10 folds was seen in 4 patients in our study with abnormal PT and serum bilirubin levels that mimicked acute viral hepatitis. El-Newihi et al. (5) showed severe hepatic derangement simulating acute viral hepatitis as rare but our study showed it happened in 4 (3.7%) patients. We think in our country where typhoid fever is endemic, in patients with high fever, relative bradycardia, jaundice, rise in transaminase and bilirubin Salmonella hepatitis is a probable diagnosis. We must consider that Salmonella hepatitis responds to proper antibiotic therapy and has an excellent prognosis.

REFERENCES

1. Osler W. Hepatic complication of typhoid fever. Johns Hopkins Hosp Rep 1899; 8: 373-87.
2. Khosla SN, Singh R, Singh GP, Trehan VK. The spectrum of hepatic injury in enteric fever. Am J Gastroenterol 1988; 83: 413-16.
3. Gitlin N. Bacterial and systemic infections. In Sciff's editor. Disease of the liver 8th ed. Lippincott William and Wilkins 1999; 1549-58.
4. Miller SI, Pegnes DA. Salmonella species, including salmonella typhi in Mandell GL, Bennett JE, Dolin R eds. Principles and practice of infectious diseases 5th ed, Churchill Livingstone 2000, 2344-57.
5. EL-Newihi HM, Alamay ME, Reynolds TB. Salmonella hepatitis, analysis of 27 cases and comparison with acute viral hepatitis. Hepatology 1996; 24: 516-19.
6. Brandborg LL, Goldman IR. Bacterial and miscellaneous infections of the liver in Zakim and Boyer eds Hepatology 2nd edition, Saunders, 1990; 1086-97.

7. Morgenstern R, Hayes PC. The liver in typhoid fever. Am J Gastroentero 1991; 86(9): 1235-39.
8. Malhiew JJ, Henning KL. Typhoid fever in New York. Arch Intern Med 1994; 154, 1713-1718.
9. Ayhan A, Gokoz A. The liver in typhoid fever. Am J Gastroenterol 1973; 59: 141-46.