UNUSUAL HEPATIC MANIFESTATIONS IN TYPHOID FEVER

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ABSTRACT

This paper deals with two patients with typhoid fever in whom hepatic manifestations were the dominant and presenting features of the illness. The ability of typhoid hepatitis to simulate other common infectious diseases in this region is highlighted. It is recommended that typhoid hepatitis should be included in the differential diagnosis of patients presenting with fever and jaundice particularly in the tropics.

Keywords: Typhoid, hepatic injury, hepatic encephalopathy, hepatic abscess.

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INTRODUCTION

Typhoid fever has been reported to involve almost all major organs of the body including the liver. This may either be a result of toxaemia or the direct effect of the salmonelleae on the organ involved[1]. While about 35% of patients have abnormal liver function tests[2], hepatomegaly has been reported in 13 to 67% of typhoid cases[1]. Jaundice, however, has been noted only in 0.5 to 8% of patients with typhoid fever[1,3,4]. In an occasional case, typhoid may present primarily with hepatic manifestations. Two such patients are now described: one with acute liver failure and hepatic encephalopathy and the other with hepatic abscess.

Case 1

A 45-year-old farmer was admitted to the hospital in November, 1987 with the provisional diagnosis of "prehepatic coma".

He was well until two weeks prior to admission when he experienced fever and vomiting. He had no bowel symptoms. The systemic review was normal. He showed no response to the erythromycin and paracetamol prescribed by his general practitioner.

On examination, he was extremely toxic with a temperature of 40°C. He was very irritable, confused and disorientated to time, place and person. He was also markedly jaundiced and dehydrated. The liver was palpable 6 cm below the right costal margin and was soft and non-tender with no bruit. The spleen was not palpable. He had no calf muscle tenderness and the eyes were not suffused. Flapping tremor could be easily elicited. He had no meningeal signs. The examination was otherwise unremarkable.

The following laboratory evaluations on admission were normal : haemoglobin, total white cell count, random blood sugar, serum electrolytes, serum creatinine phosphakinase (CPK), chest x-ray and urinalysis. The blood urea was at the upper limit of normal at 8.4 mmol/l. The liver function test (LFT) results are given in Table I.

The septic workup including blood, stool and urine cultures as well as the peripheral blood films for malarial parasites were negative.

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He was initially thought to suffer from "prehepatic coma complicating viral hepatitis". The possibility of leptospirosis too was entertained.

He was rehydrated with intravenous fluids. He was then treated with a combination of intravenous crystalline penicillin, gentamycin and metronidiazole with oral neomycin and lactulose. There was no response to this treatment. His condition deteriorated with swinging temperature and clouding of consciousness.

Meanwhile the Widal agglutination tests for "TO" and "TH" antigens showed positive titres at 1/50 and 1/800 dilutions respectively. These titres for "TO" and "TH" rose to 1/200 and 1/4000 respectively on repeating the tests a week later.

The microscopic agglutination test for leptospirosis was negative.

An ultrasound examination of the abdomen at this stage was normal.

His aforementioned medications were stopped after a week. He was then started on a two week course of chloramphenicol; given parenterally initially.

His general condition improved rapidly. The confusional state cleared within the next few days and the temperature settled on the sixth day of chloramphenicol therapy. He was discharged home three weeks later when his liver function tests were normal. He remains well two years later.

Case 2

A 44-year-old customs officer was admitted to the hospital in October 1989 for fever.

He was in excellent health till about four days prior to admission when he experienced abrupt onset of fever with chills and rigors. He also developed constipation. The history was otherwise unremarkable.

Physical examination revealed a jaundiced, toxic and ill looking man with a temperature of 39.5°C. The liver was just felt below the right costal margin and was soft and non-tender. The examination was otherwise normal.

The routine laboratory counts and septic workup mentioned for the first patient were also done for this patient. They were either normal or negative. The LFT results are shown in Table I. In addition, the Widal reaction was negative on admission.

He was given a course of chloroquine and doxycycline in turn for the possibilities of malaria and scrub typhus respectively. There was no response to these therapeutic trials.

The Widal agglutination tests repeated a week later were positive for "TO" and "TH" at 1/400 each respectively.

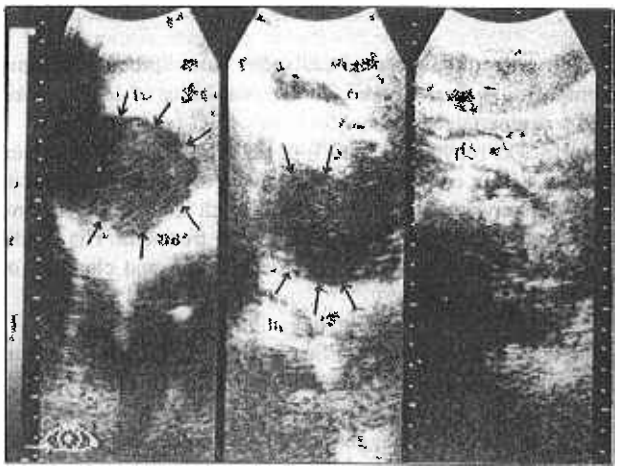
An ultrasound examination of the abdomen done at this stage showed an unifocal abscess measuring "64 x 75 x 54 mm in the posterosuperior aspect of the right lobe of the liver". (Fig 1).

He was given a two week course of chloramphenicol therapy. There was prompt response. There was rapid

Table I
Liver Function Tests

Patient		1	2	Normal values		
Serum Bilirubin	:	233	48	micromole/l	(3 - 18.8	micromole/l)
Serum Albumin	:	26	43	(G/L)	(35 - 48	G/L)
Serum Globulin	:	35	33		(23 - 36	G/L)
Serum Alkaline phosphatase	:	17.6	15		(3 - 13	K.A. units/L)
Alanine transaminase (ALT)	:	43	65	(R.F. units)	(4 - 30	R.F. units)
Hepatitis B surface antigen	:	negative	negative			

Fig 1 – Ultrasound film showing hepatic abscess (arrowed).



improvement in his general condition with the temperature settling on the seventh day of chloramphenicol. The liver function tests became normal over the next few weeks. A repeat ultrasound examination done three weeks later showed complete resolution of the abscess. He remains well eight months later.

DISCUSSION

Typhoid was not considered seriously at the time of presentation in both the patients. In the first case, the acute liver failure and hepatic encephalopathy were thought to be complications of underlying viral hepatitis. However, the absence of prodromal symptoms preceding the onset of jaundice and mildly elevated transaminases made viral hepatitis less likely in both the cases. Moreover, fever usually subsides after the appearance of icterus in viral hepatitis[5]. The markedly raised bilirubin levels with minimally raised AST levels too excluded viral hepatitis.

Leptospirosis was the other possibility entertained in Case 1 initially. The absence of suffused eyes and muscle tenderness with normal CPK levels and urinalysis[6] spelt against that diagnosis. The serological test for leptospirosis was later found to be negative.

Malaria and scrub typhus could not be excluded confidentially on clinical grounds in the second patient. Thus he was given therapeutic trials for these infections to which he did not respond.

The final diagnosis of typhoid fever was provided by the Widal reaction in both the patients. The initial test was strongly positive in the first case while both the patients showed the characteristic rise in titres when the tests were repeated later.

The blood cultures were negative for salmonella typhi in both cases. This was probably due to previous antibiotic therapy in the first patient. The reason for the negative cultures in the second case is not clear. However, the negative cultures in both cases are not surprising. In Ramachandran et al's series of 92 patients with typhoid hepatitis, 51 cases (55%) were found to be culture negative with positive Widal reaction[3]. This appears to be the experience of other workers too[7]. The excellent response to chloramphenicol therapy by the two patients has been observed to be a feature of typhoid hepatitis in earlier studies[7].

Typhoid presenting with acute liver failure and hepatic encephalopathy, appears to be rare. There was one report earlier in which the patient in addition also had acute renal failure secondary to typhoid nephritis and thrombocytopaenia[8].

In the second patient, typhoid liver abscess was not suspected clinically. The ultrasound examination was done mainly to explore the possibility of ascending cholangitis or gallstones. Surprisingly it showed hepatic abscess (Fig 1). Salmonella hepatic abscess had been reported as early as in 1911 by Von Eberts. Recently two cases of typhoid hepatic abscess in children were reported[9]. Unlike our second patient in whom the abscess resolved with chloramphenicol alone, these children required percutaneous drainage of the abscesses in addition to antibiotics.

The pathogenesis of typhoid hepatitis is unclear[4]. It has been pointed out that this entity is more likely in patients who were already anaemic, malnourished and in poor health[1]. This was not the case in our patients. It has also been postulated that the hepatic abscess in typhoid may be primarily due to haematogenous spread of the organism to the liver[9].

Whatever the pathophysiology may be, it is necessary to recognise typhoid hepatitis as a distinct entity as it is easily amenable to treatment. As illustrated by our patients, typhoid hepatitis can simulate a variety of common infections viz viral and malarial hepatitis, leptospirosis and scrub typhus. It is to be noted that the above infectious diseases are common in the same location where typhoid is an endemic problem[3] as in our region.

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